Harris, A.
09/807575

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DICTIONARY FILE UPDATES: 15 MAR 2006 HIGHEST RN 877033-93-7

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* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
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http://www.cas.org/ONLINE/UG/regprops.html

- key terms

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               E "GLYPICAN-1"/CN
               E GLYPICAN 1/CN
L1           2 S E4-5
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FILE 'CAPLUS' ENTERED AT 17:31:38 ON 16 MAR 2006
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FILE COVERS 1907 - 16 Mar 2006 VOL 144 ISS 12
FILE LAST UPDATED: 15 Mar 2006 (20060315/ED)

Searcher : Shears 571-272-2528

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http://www.cas.org/infopolicy.html

L1 2 SEA FILE=REGISTRY ABB=ON PLU=ON ("GLYPICAN 1 (HUMAN)"/CN OR "GLYPICAN 1 (MOUSE STRAIN C57BL/6 CLONE MGC:86094 IMAGE:6810413)"/CN)
L2 3313 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR GLYPICAN(1W)(1 OR I) OR HSPG OR HEPARAN(W)(SULFATE OR SULPHATE)(W)(PROTEOGLYCAN OR PROTEO GLYCAN) OR (PROTEOHEPARAN OR PROTEO HEPARAN)(W)(SULFATE OR SULPHATE)
L5 14 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND (DIAGNOS? OR DETECT? OR DET## OR DETERM? OR SCREEN?)(S)((CANCER? OR CARCIN? OR TUMOUR OR TUMOR OR NEOPLAS?)(10A)(BREAST OR MAMMAR? OR PANCREAT? OR PANCREAS))

L5 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Aug 2005
ACCESSION NUMBER: 2005:862206 CAPLUS
DOCUMENT NUMBER: 144:45101
TITLE: Evaluation of leukocyte arylsulphatase A, serum interleukin-6 and urinary heparan sulphate following tamoxifen therapy in breast cancer
AUTHOR(S): Oener-Iyidogan, Yildiz; Oener, Pernur; Kocak, Hikmet; Lama, Abdul; Guerdoel, Figen; Bekpinar, Seldag; Unur, Nurettin; Oezbek-Kir, Zeynep
CORPORATE SOURCE: Istanbul Faculty of Medicine, Department of Biochemistry, Istanbul University, Istanbul, 34093, Turk.
SOURCE: Pharmacological Research (2005), 52(4), 340-345
CODEN: PHMREP; ISSN: 1043-6618
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Leukocyte arylsulphatase A (AS-A) was shown to be significantly high in newly-**diagnosed breast cancer** patients. Previous reports imply a connection between serum interleukin-6 (IL-6) and breast cancer, possibly through a modulation of enzymes involved in estrogen synthesis. Abnormal distribution of **heparan sulfate proteoglycans** (**HSPGs**) in malignant breast epithelial cells suggests that they play a key role in the regulation of cell growth. Estradiol is believed to be effective in modulating glycosaminoglycans (GAGs) and their depolymg. enzymes. Therefore, in this study, attempts were made to evaluate the activity of leukocyte arylsulphatase A, serum interleukin-6, urinary GAGs and heparan sulfate (HS) in response to tamoxifen (TAM) therapy in mastectomized breast cancer patients. Thirty-four patients (aged 30-82 years) were administered TAM (20 mg twice daily). Blood and urine samples of each patient were collected three times (at the beginning, and in third and sixth month of TAM therapy), and biochem. parameters were measured. There was no difference between baseline leukocyte AS-A activity and that measured after three months. At the end of six months, enzyme activity was significantly higher than the former values ($p = 0.022$), but within the reference intervals reported in the literature. Although this increase might imply a normalization, the duration of TAM therapy is not long enough to make a decision about either regression or aggravation of

the disease. TAM did not have any effect on serum IL-6, urinary HS and GAG levels which may be due to insensitivity of these variables to TAM during the short period of therapy. Both urinary GAG and HS levels measured at sixth month exhibited a pos. correlation with the baseline level of leukocyte AS-A (p = 0.005 and 0.009, resp.), suggesting that pos. responses to the drug might be seen in patients with low AS-A activity.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 29 Jul 2005
ACCESSION NUMBER: 2005:671727 CAPLUS
DOCUMENT NUMBER: 143:166667
TITLE: The curcuminoids- and anthocyanins-responsive genes in human adipocytes and their use in screenings of anti-obesity and anti-diabetes drugs
INVENTOR(S): Ueno, Yuki; Tsuda, Takanori; Takanori, Hitoshi; Yoshikawa, Toshikazu; Osawa, Toshihiko
PATENT ASSIGNEE(S): Biomarker Science Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 85 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005198640	A2	20050728	JP 2004-53258	20040227
PRIORITY APPLN. INFO.:			JP 2003-394758 A	20031125

AB The curcuminoids- and anthocyanins-responsive gene expression profiles in adipocytes have been revealed. The curcuminoids- and anthocyanins-responsive genes are designed to be used as the index markers in the screenings of the substances that can affect the gene expression patterns in obesity and diabetes. These substances can be the candidates of anti-obesity and anti-diabetes drugs. Therefore, the groups of curcuminoids- and anthocyanins-responsive genes are intended to be used as markers in a form of kit such as DNA chip for the screening of anti-obesity and anti-diabetes drugs.

L5 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 2005
ACCESSION NUMBER: 2005:404045 CAPLUS
DOCUMENT NUMBER: 143:403402
TITLE: Enhanced levels of Hsulf-1 interfere with heparin-binding growth factor signaling in pancreatic cancer
AUTHOR(S): Li, Junsheng; Kleeff, Joerg; Abiatari, Ivane; Kayed, Hany; Giese, Nathalia A.; Felix, Klaus; Giese, Thomas; Buechler, Markus W.; Friess, Helmut
CORPORATE SOURCE: Department of General Surgery, University of Heidelberg, Heidelberg, Germany
SOURCE: Molecular Cancer (2005), 4, No pp. given
CODEN: MCOACG; ISSN: 1476-4598
URL: http://www.molecular-cancer.com/content/pdf/1476-4598-4-14.pdf

PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Hsulf-1 is a newly identified enzyme, which has the ability to decrease the growth of hepatocellular, ovarian, and head and neck squamous cell carcinoma cells by interfering with heparin-binding growth factor signaling. Since pancreatic cancers overexpress a number of heparin-binding growth factors and their receptors, the expression and function of this enzyme in pancreatic cancer was analyzed. Results: **Pancreatic cancer** samples expressed significantly (22.5-fold) increased Hsulf-1 mRNA levels compared to normal controls, and Hsulf-1 mRNA was localized in the cancer cells themselves as well as in peritumoral fibroblasts, 4 out of 8 examined **pancreatic cancer** cell lines expressed Hsulf-1, whereas its expression was below the level of **detection** in the other cell lines. Stable transfection of the Hsulf-1 neg. Panc-1 pancreatic cancer cell line with a full length Hsulf-1 expression vector resulted in increased sulfatase activity and decreased cell-surface **heparan-sulfate proteoglycan** (**HSPG**) sulfation. Hsulf-1 expression reduced both anchorage-dependent and -independent cell growth and decreased FGF-2 mediated cell growth and invasion in this cell line. Conclusion: High expression of Hsulf-1 occurs in the stromal elements as well as in the tumor cells in pancreatic cancer and interferes with heparin-binding growth factor signaling.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 31 Jan 2005
ACCESSION NUMBER: 2005:80419 CAPLUS
DOCUMENT NUMBER: 142:461049
TITLE: Correlation of Expression of Heparanase with Angiogenesis and Prognosis of Breast Cancer
AUTHOR(S): Liu, Zhenzhen; Zhang, Hengwei; Wei, Bing; Cui, Shude
CORPORATE SOURCE: Department of Breast, Henan Provincial Tumor Hospital, Zhengzhou, Henan Province, 450008, Peop. Rep. China
SOURCE: Aizheng (2004), 23(11), 1342-1345
CODEN: AIZHE4; ISSN: 1000-467X
PUBLISHER: Sun Yat-sen Daxue, Aizheng Zhongxin
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Heparanase is a **heparan sulfate proteoglycan** cleaving enzyme. It helps to degrade extracellular matrix and basement membrane, promote angiogenesis, and accelerate tumor metastasis. This study was to investigate correlation of heparanase expression with angiogenesis and prognosis of breast cancer. Immunohistochem. was used to **detect** heparanase and microvessel d. (MVD) in 120 specimens of infiltrative ductal **breast cancer**, and 20 specimens of normal **breast** tissue. The correlations of heparanase expression with clinicopathol. factors and prognosis of breast cancer were analyzed using Chi-square test, t test, Kaplan-Meier method, and log-rank test. The results showed that the pos. rate of heparanase in breast cancer was 65% (78/120), which was significantly higher than that in the normal breast tissue (0, 0/10). MVD in breast cancer was

53.84±13.45, which was significantly higher than that in the control group (33.32±8.55). The expression of heparanase was pos. correlated with tumor size, histol. grade, lymph node metastasis, and clin. stage of breast cancer, and neg. correlated with 5-yr survival rate. MVD in the heparanase pos. group was much higher than the that in heparanase neg. group, and MVD was pos. correlated with heparanase expression (r=0.358, P<0.01). Heparanase may promote angiogenesis, and may be closely correlated with prognosis of breast cancer.

L5 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 17 Dec 2004
ACCESSION NUMBER: 2004:1081081 CAPLUS
DOCUMENT NUMBER: 142:69928
TITLE: Differentially regulated hepatocellular carcinoma genes and protein and DNA arrays for use in diagnosis and drug screening
INVENTOR(S): Ren, Ee Chee; Neo, Soek Ying
PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108964	A1	20041216	WO 2004-SG166	20040604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1631682	A1	20060308	EP 2004-736172	20040604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-475508P P 20030604
WO 2004-SG166 W 20040604

AB The invention provides genes differentially expressed in hepatocellular carcinoma (HCC) as well as DNA and protein arrays which may be used for HCC diagnosis, to assess HCC progression or regression, or the efficacy and/or toxicity of HCC therapeutics, and/or to identify candidate compds. for HCC therapy, with high predictive accuracy.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 06 Jun 2003
ACCESSION NUMBER: 2003:435071 CAPLUS
DOCUMENT NUMBER: 139:3235
TITLE: **Glypican-1 determination** and modulation in human **breast cancer diagnosis** and treatment
INVENTOR(S): Korc, Murray; Lander, Arthur D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U. S. Ser. No. 807,575.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003103980	A1	20030605	US 2002-210327	20020731
WO 2000023109	A1	20000427	WO 1999-US24176	19991015

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:			
US 1998-104510P	P	19981016	
US 1999-121624P	P	19990225	
WO 1999-US24176	W	19991015	
US 2001-807575	A2	20010712	
US 2001-309722P	P	20010731	

AB Glycosylphosphatidylinositol- (GPI-) anchored **heparan sulfate proteoglycan** (**HSPG**) **glypican-1** is strongly expressed in human breast and pancreatic cancer-both by the cancer cells and, in the case of pancreatic cancer, the adjacent fibroblasts-whereas expression of **glypican-1** is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic cancer cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in breast cancer tissues as well as breast cancer cells by comparison with breast normal tissues. Temporary or permanent transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein

levels and the mitogenic response to FGF2 and HB-EGF. Glypican can be used to detect the carcinoma in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense constructs) of surface of the extracellular domain of **glypican-1** are effective in retarding the growth of glypican-responsive carcinomas. By immunohistochem., strong **glypican-1** immunoreactivity was present in a heterogeneous pattern in the cancer cells forming intraductal and lobular carcinomas, and in the fibroblasts surrounding the cancer cells but not in the fibroblasts that were more distant from the tumor. A moderate to strong **glypican-1** mRNA in situ hybridization signal was also present in the cancer cells, and, to a lesser extent, in the fibroblasts immediately adjacent to the cancer cells. These observations suggest that breast cancer cells produce and release **glypican-1**, and that some of the **glypican-1** present in the fibroblasts surrounding the breast cancer cells in vivo derives from the cancer cells.

L5 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 May 2003
ACCESSION NUMBER: 2003:362860 CAPLUS
DOCUMENT NUMBER: 139:144162
TITLE: Fibroblast growth factor 7, secreted by breast fibroblasts, is an interleukin-1β-induced paracrine growth factor for human breast cells
AUTHOR(S): Palmieri, C.; Roberts-Clark, D.; Assadi-Sabet, A.; Coope, R. C.; O'Hare, M.; Sunters, A.; Hanby, A.; Slade, M. J.; Gomm, J. J.; Lam, E. W.-F.; Coombes, R. C.
CORPORATE SOURCE: Cancer Research UK Laboratories, Department of Cancer Medicine, Imperial College, Hammersmith Hospital, London, W12 0NN, UK
SOURCE: Journal of Endocrinology (2003), 177(1), 65-81
CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Keratinocyte growth factor/fibroblast growth factor 7 (KGF/FGF7) is known to be a potent growth factor for mammary cells but its origin, cellular targets and mode of action in the breast are unclear. In this study, the authors carried out studies to determine the localization of FGF7 and its receptor, and the related growth factor FGF10. The authors also **determined** the factors that regulate FGF7 release from stromal cells and the effects of FGF7 on normal and **neoplastic breast** cells. Using an FGF7-specific antibody which does not react with the FGF7 **heparan sulfate proteoglycan** (**HSPG**)-binding site, the authors showed epithelial and myoepithelial immunohistochem. staining in normal breast sections, and epithelial staining in breast carcinomas. Stromal staining was also detected in some lobular carcinomas as well as a subset of invasive ductal carcinomas. FGF10 and FGF receptor (FGFR)2 immunostaining showed a similar epithelial expression pattern, whereas no stromal staining was observed The authors purified normal breast stromal, epithelial and myoepithelial cells and showed that FGF7 stimulated proliferation of both epithelial cell types, but not stromal fibroblasts. The authors also examined the effects of FGF7 on Matrigel-embedded organoids, containing both epithelial and myoepithelial cells, and showed FGF7 induced an increase in

cellular proliferation. Furthermore, conditioned medium derived from stromal cells was shown to increase the proliferation of normal and neoplastic breast epithelial cells, which could be abolished by a neutralizing antibody to FGF7. Finally, the authors showed that interleukin-1β, but not estradiol or other estrogen receptor ligands, caused a dose-related FGF7 release. Further results also indicate that the epithelial localization of FGF7 and FGF10 in breast tissue sections is likely to be due to their binding to their cognate receptor. In summary, the authors' findings suggest that FGF7 is a paracrine growth factor in the breast. FGF7 is produced by the breast stromal fibroblasts and has profound proliferative and morphogenic roles on both epithelial and myoepithelial cells.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 15 Jan 2003
ACCESSION NUMBER: 2003:33516 CAPLUS
DOCUMENT NUMBER: 138:335272
TITLE: Methylation-associated silencing of heparan sulfate D-glucosaminyl 3-O-sulfotransferase-2 (3-OST-2) in human breast, colon, lung and pancreatic cancers
AUTHOR(S): Miyamoto, Kazuaki; Asada, Kiyoshi; Fukutomi, Takashi; Okochi, Eriko; Yagi, Yukiko; Hasegawa, Tadashi; Asahara, Toshimasa; Sugimura, Takashi; Ushijima, Toshikazu
CORPORATE SOURCE: Carcinogenesis Division, National Cancer Center Research Institute, 1-1 Tsukiji 5-chrome, Chuo-ku, Tokyo, 104-0045, Japan
SOURCE: Oncogene (2003), 22(2), 274-280
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aberrant CpG methylations play important roles in cancer development and progression. In this study, aberrant methylations in human breast cancer were searched for using methylation-sensitive representational difference anal. (MS-RDA). A CpG island (CGI) in the 5' region of the heparan sulfate D-glucosaminyl 3-O-sulfotransferase-2 (3-OST-2) gene was found to be hypermethylated, while its exon 2 was hypomethylated. In seven breast cancer cell lines, hypermethylation of the 5' region and loss of 3-OST-2 expression were observed Treatment with a demethylating agent, 5-aza-2'-deoxycytidine, removed the methylation of the CGI in the 5' region and restored its expression, demonstrating silencing of the 3-OST-2 gene. Methylation-specific PCR (MSP) anal. in 85 primary breast cancers showed that the hypermethylation of the CGI in the 5' region was present in 75 (88%) of them. Quant. reverse transcriptase-PCR (RT-PCR) anal. in 37 primary breast cancers showed that the average expression level was decreased in them. Further, MSP anal. in primary colon, lung and pancreatic cancers showed that hypermethylation of the CGI in the 5' region was present in the colon (8/10, 80%), lung (7/10, 70%) and pancreatic (10/10, 100%) cancers. These results showed that silencing of 3-OST-2 was present in a wide range of human cancers. The 3-OST-2 gene encodes an enzyme involved in the final modification step of **heparan sulfate proteoglycans** (**HSPGs**), and its silencing is expected to result in abnormal modification of **HSPGs** and abnormal

signal transduction. From the high incidence, silencing of the 3-OST-2 gene is expected to have high diagnostic, and potentially therapeutic, values.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 10 Dec 2002
ACCESSION NUMBER: 2002:937303 CAPLUS
DOCUMENT NUMBER: 138:20443
TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Bio Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2002355079	A2	20021210	JP 2002-69354		20020313
PRIORITY APPLN. INFO.:			JP 2001-73183	A	20010314
			JP 2001-74993	A	20010315
			JP 2001-102519	A	20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

L5 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 30 Jan 2002
ACCESSION NUMBER: 2002:79328 CAPLUS
DOCUMENT NUMBER: 137:61142
TITLE: **Heparan sulfate proteoglycans** as regulators of fibroblast growth factor-2 receptor binding in breast carcinomas
AUTHOR(S): Mundhenke, Christoph; Meyer, Kristy; Drew, Sally; Friedl, Andreas
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine,

University of Wisconsin-Madison, Madison, WI, USA
SOURCE: American Journal of Pathology (2002), 160(1), 185-194
CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER: American Society for Investigative Pathology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Binding of fibroblast growth factors (FGFs) to their tyrosine kinase-signaling receptors (FGFRs) requires heparan sulfate (HS). HS proteoglycans (**HSPGs**) **determine** mitogenic responses of **breast carcinoma** cells to FGF-2 in vitro. For this study, we examined the role of **HSPGs** as modulators of FGF-2 binding to FGFR-1 in situ and in vitro. During stepwise reconstitution of the FGF-2/**HSPG**/FGFR-1 complex in situ, we identified an elevated ability of breast carcinoma cell **HSPGs** to promote receptor complex formation compared to normal breast epithelium. **HSPGs** isolated from the MCF-7 breast-carcinoma cell line were then fractionated according to their ability to assemble the FGF-2 receptor complex. All MCF-7 **HSPGs** are decorated with HS chains similarly capable of promoting FGF-2 receptor complex formation. In this in vitro model, syndecan-1 and syndecan-4 are the cell surface **HSPGs** contributing most to the complex formation. Relative expression levels of these syndecans in human **breast carcinoma** tissues correlate well with receptor complex formation in situ, indicating that in **breast carcinomas**, core protein levels **determine** FGF-2 receptor complex formation. However, variances in syndecan expression levels do not explain the difference in FGF-2 receptor complex formation between normal and malignant epithelial cells, suggesting that alterations in HS structure occur during malignant transformation.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 27 Jul 2001
ACCESSION NUMBER: 2001:544238 CAPLUS
DOCUMENT NUMBER: 135:240061
TITLE: **Glypican-1** is overexpressed in human breast cancer and modulates the mitogenic effects of multiple heparin-binding growth factors in breast cancer cells
AUTHOR(S): Matsuda, Kei; Maruyama, Haruhisa; Guo, Fang; Kleeff, Jorg; Itakura, Jun; Matsumoto, Yoshiro; Lander, Arthur D.; Korc, Murray
CORPORATE SOURCE: Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Biological Chemistry, University of California, Irvine, CA, 92697, USA
SOURCE: Cancer Research (2001), 61(14), 5562-5569
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glypicans are a family of glycosylphosphatidylinositol-anchored cell surface **heparan sulfate proteoglycans** implicated in the control of cellular growth and differentiation. Here we show that **glypican-1** is strongly expressed in human breast cancers, whereas expression of **glypican-**

1 is low in normal breast tissues. In contrast, the expression of glypican-3 and -4 is only slightly increased in **breast cancers** by comparison with normal **breast** tissues, and glypican-2 and -5 are below the level of **detection** by Northern blotting in both normal and cancer samples. Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with phosphoinositide-specific phospholipase-C abrogated the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor and fibroblast growth factor 2. Stable transfection of these cells with a **glypican -1** antisense construct markedly decreased **glypican -1** protein levels and the mitogenic response to the same heparin-binding growth factors, as well as that to heregulin α, heregulin β, and hepatocyte growth factor. Syndecan-1 was also expressed at high levels in both breast cancer tissues and breast cancer cells when compared with normal breast tissues. There was a good correlation between **glypican-1** and syndecan-1 expression in the tumors. However, clones expressing the **glypican-1** antisense construct did not exhibit decreased syndecan-1 levels, indicating that loss of responsiveness to heparin-binding growth factors in these clones was not due to altered syndecan-1 expression. Furthermore, 8 of 10 tumors with stage 2 or 3 disease exhibited high levels of **glypican-1** by Northern blot anal. In contrast, low levels of **glypican-1** mRNA were evident in 1 of 10 tumors with stage 2 or 3 disease and in 9 of 10 tumors with stage 1 disease. Taken together, these data suggest that **glypican-1** may play a pivotal role in the ability of breast cancer cells to exhibit a mitogenic response to multiple heparin-binding growth factors and may contribute to disease progression in this malignancy.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 28 Apr 2000
ACCESSION NUMBER: 2000:277880 CAPLUS
DOCUMENT NUMBER: 132:305482
TITLE: Glypicans for the detection and treatment of human carcinoma
INVENTOR(S): Lander, Arthur; Korc, Murray
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023109	A1	20000427	WO 1999-US24176	19991015

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346264		AA	20000427	CA 1999-2346264	19991015
EP 1146903		A1	20011024	EP 1999-954963	19991015
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 769125		B2	20040115	AU 2000-11181	19991015
US 2003103980		A1	20030605	US 2002-210327	20020731
PRIORITY APPLN. INFO.:				US 1998-104510P	P 19981016
				US 1999-121624P	P 19990225
				WO 1999-US24176	W 19991015
				US 2001-807575	A2 20010712
				US 2001-309722P	P 20010731

AB Glycosylphosphatidylinositol- (GPI-) anchored **HSPG glypican-1** is strongly expressed in human breast and pancreatic cancer - both by the cancer cells and in the case of pancreatic cancer the adjacent fibroblasts - whereas expression of **glypican-1** is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic cancer cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in breast cancer tissues as well as breast cancer cells by comparison with breast normal tissues. Temporary or permanent transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein levels and the mitogenic response to FGF2 and HB-EFG. Glypican can be used to detect the carcinoma in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense constructs) of surface of the extracellular domain of **glypican-1** are effective in retarding the growth of glypican-responsive carcinomas.

IT **131753-81-6, Glypican 1,** human
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(glypicans for detection and treatment of human carcinoma)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Jan 2000
ACCESSION NUMBER: 2000:53938 CAPLUS
DOCUMENT NUMBER: 132:102821
TITLE: Method of screening for potential anti-metastatic and anti-inflammatory agents using mammalian heparanase as a probe
INVENTOR(S): Ben-Artzi, Hanna; Ayal-Hershkovitz, Maty; Vlodavsky, Israel; Pecker, Iris; Peleg, Yoav;

Miron, Daphna
PATENT ASSIGNEE(S): Insight Strategy & Marketing Ltd., Israel; Hadasit Medical Research Services & Development Ltd.; Friedman, Mark M.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000003036	A1	20000120	WO 1999-US15643	19990712
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6190875	B1	20010220	US 1998-113168	19980710
CA 2335382	AA	20000120	CA 1999-2335382	19990712
AU 9948697	A1	20000201	AU 1999-48697	19990712
AU 758485	B2	20030320		
EP 1097241	A1	20010509	EP 1999-932382	19990712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002520029	T2	20020709	JP 2000-559256	19990712
NO 2001000136	A	20010309	NO 2001-136	20010109
AU 2001069997	A5	20011206	AU 2001-69997	20010911
AU 772311	B2	20040422		
AU 2003242497	A1	20030925	AU 2003-242497	20030829
AU 2004201431	A1	20040513	AU 2004-201431	20040406
AU 2004201462	A1	20040506	AU 2004-201462	20040408

PRIORITY APPLN. INFO.:	US 1998-113168	A	19980710
	US 1997-922170	A2	19970902
	US 1998-109386	B2	19980702
	AU 1998-91258	A3	19980831
	WO 1999-US15643	W	19990712
	AU 2000-29881	A3	20000210
	AU 2001-69997	A	20010911

AB Qual. and quant. methods are provided for testing an agent for its potential at inhibiting glycosidase catalytic activity, the methods including interacting a glycosidase enzyme with a glycosidase substrate in a presence of the agent and qual. or quant. evaluating an effect of the agent on the catalytic activity of the glycosidase enzyme toward the glycosidase substrate. Preferably the glycosidase enzyme is a heparanase enzyme and the glycosidase substrate is, resp., a heparanase substrate.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L5 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 09 Apr 1998
ACCESSION NUMBER: 1998:200677 CAPLUS
DOCUMENT NUMBER: 128:268949
TITLE: Gene expression and protein deposition of major basement membrane components and TGF-β1 in human breast cancer
AUTHOR(S): Nerlich, Andreas G.; Wiest, Irmgard; Wagner, Evi; Sauer, Ulrich; Schleicher, Erwin D.
CORPORATE SOURCE: Pathologisches Institut der Universitat Munchen, Munchen, D-80337, Germany
SOURCE: Anticancer Research (1997), 17(6D), 4443-4449
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Here, the authors used immunohistochem. and in-situ hybridization for the localization of major basement membrane (BM) components and their mRNA, resp., to **determine** the extent of BM production and deposition in normal **mammary** tissue as well as in invasive **mammary carcinomas**. While normal mammary tissue showed an intact epithelial BM, as evidenced by a continuous linear staining for collagen IV, laminin, **heparan sulfate proteoglycan** (perlecan) and fibronectin, this staining was widely lost in the invasive carcinomas. Non-invasive intraductal areas of the carcinomas (carcinoma-in-situ) revealed focal fragmentation and duplication of the epithelial BM. Using in-situ hybridization, the authors observed only focally pos. mRNA-expression for collagen IV-, perlecan-, and fibronectin-mRNA in normal glands, while mRNA-signals were enhanced in one case of fibroadenoma and particularly in invasive and non-invasive carcinomas, regardless of the degree of tumor cell differentiation. In these instances both tumor and stroma cells were pos. labeled. In addition, the authors could demonstrate an increase in the level of TGF-β1-mRNA, as the most active cytokine for the induction of matrix component production, by carcinoma cells and to lesser extent by stroma cells. The discrepancy between enhanced mRNA-synthesis and loss in protein deposition points either to an upregulated activity of matrix degrading proteinases (matrix-metalloproteinases) or a posttranslational block of protein synthesis or both.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'MEDLINE' ENTERED AT 17:31:41 ON 16 MAR 2006

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FILE 'JAPIO' ENTERED AT 17:31:41 ON 16 MAR 2006
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L6 37 S L5
L7 17 DUP REM L6 (20 DUPLICATES REMOVED)

L7 ANSWER 1 OF 17 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:144377 SCISEARCH
THE GENUINE ARTICLE: 009IC
TITLE: Predictive value of syndecan-1 expression for the response to neoadjuvant chemotherapy of primary breast cancer
AUTHOR: Gotte M (Reprint); Kersting C; Ruggiero M; Tio J; Tulusan A H; Kiesel L; Wulfing P
CORPORATE SOURCE: Munster Univ Hosp, Dept Obstet & Gynecol, Albert Schweitzer Str 33, D-48129 Munster, Germany (Reprint); Munster Univ Hosp, Dept Obstet & Gynecol, D-48129 Munster, Germany; Munster Univ Hosp, Dept Pathol, D-48129 Munster, Germany; Klinikum Bayreuth, Dept Obstet & Gynecol, Bayreuth, Germany; Univ Pisa, Dept Reprod Med & Child Dev, I-56100 Pisa, Italy
mgotte@uni-muenster.de
COUNTRY OF AUTHOR: Germany; Italy
SOURCE: ANTICANCER RESEARCH, (JAN-FEB 2006) Vol. 26, No. 1B, pp. 621-627.
ISSN: 0250-7005.
PUBLISHER: INT INST ANTICANCER RESEARCH, EDITORIAL OFFICE 1ST KM KAPANDRITIOU-KALAMOU RD KAPANDRITI, PO BOX 22, ATHENS 19014, GREECE.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 26
ENTRY DATE: Entered STN: 16 Feb 2006
Last Updated on STN: 16 Feb 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: The overexpression of syndecan-1 in breast carcinomas correlates with poorer prognosis and an aggressive phenotype. The effect of syndecan-1 expression on **tumor** response to neoadjuvant chemotherapy was **determined** in locally advanced **breast cancer**. Patients and Methods: Semi-quantitative syndecan-1 immunohistochemistry was performed in pre-chemotherapy breast cancer biopsies of 37 patients undergoing high-dose neoadjuvant treatment with cyclophosphamide and epirubicin. Results: 43.2% of breast carcinomas stained positive for syndecan-1. Syndecan-1 expression was more frequent in ductal invasive carcinomas than in other histological types (p=0.062). The pathological response to chemotherapy was decreased in syndecan-1-positive patients: 37.5% of syndecan-1-positive vs. 19% of syndecan-1-negative patients attained pathologically "no change". No syndecan-1-positive patient showed complete remission. Also, a correlation between syndecan-1

immunostaining intensity and response to chemotherapy was observed. Of the responding tumors, none showed strong syndecan-1 expression (Score 3+), whereas 20% of the non-responding tumors were strongly syndecan-1-positive. Conclusion: Syndecan-1-expressing breast carcinomas show a trend towards a decreased response to chemotherapy.

L7 ANSWER 2 OF 17 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-202311 [21] WPIDS
DOC. NO. CPI: C2005-167670
TITLE: Identification of angiopoietin activity, involves contacting endothelial cells with cells comprising angiopoietin in presence of test compound, determining level of integrity loss, and comparing determined level with standard level.
DERWENT CLASS: B04 D16
INVENTOR(S): XU, Y; YU, Q
PATENT ASSIGNEE(S): (UYPE-N) UNIV PENNSYLVANIA
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005013890	A2	20050217	(200521)*	EN	86

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005013890	A2	WO 2004-US16808	20040528

PRIORITY APPLN. INFO: US 2003-479802P 20030619; US 2003-473998P 20030529

AN 2005-202311 [21] WPIDS

AB WO2005013890 A UPAB: 20060116
NOVELTY - Identification of angiopoietin-3 (Ang-3) activity involves contacting endothelial cells with cells comprising Ang-3 in presence of a test compound, determining specific parameters, and comparing the level with standard level. The reduction in the level of endothelial cell retraction, loss of integrity, and increase in level of proliferation/reduction in the level of apoptosis indicates the test compound inhibits Ang-3.

DETAILED DESCRIPTION - Identification of angiopoietin-3 (Ang-3) activity involves contacting endothelial cells with cells comprising Ang-3 in presence of a test compound, determining the parameters such as level of endothelial cell retraction, loss of integrity and proliferation/level of apoptosis, and comparing the determined level with standard level observed when the endothelial cells are contacted with cells comprising Ang-3 bound with **HSPG** in absence of test compound. The reduction in the level of endothelial cell retraction, loss of integrity, and increase in the level of

proliferation or reduction in the level of apoptosis indicates that the test compound inhibits Ang-3.

INDEPENDENT CLAIMS are also included for the following:

(1) identification of modulators of Ang-3 binding with **HSPGs**;

(2) treatment of cancer, arthritis, diabetes, vascular disease, stroke/angioplasty, which involves administering Ang-3 or nucleic acid molecule encoding Ang-3 in an expressible vector;

(3) method of blocking endothelial cell proliferation and inhibiting endothelial cell retraction or loss of integrity, which involves delivering Ang-3 inhibitor to the endothelial cell;

(4) method of anchoring a protein to cell surface;

(5) diagnosis of restenosis, atherosclerosis, hemorrhage and stroke;

(6) method of developing prognosis for individual diagnosed with restenosis, atherosclerosis, hemorrhage heart attack and stroke; and

(7) identification of inhibitors of Ang-4 activity.

ACTIVITY - Cytostatic; Antiangiogenic; Antiarthritic; Antidiabetic; Vasotropic; Antiarteriosclerotic; Cerebroprotective. Test details are given but no results given.

MECHANISM OF ACTION - Angiogenesis-Inhibitor; Apoptosis-Stimulator. Brdu-labeled HUVECs were seeded into 24-well plates in triplicate (5 multiply 104 cells/well) and cultured for 4 hours and switched to SFM for 8 hours. Fresh SFM or SFM containing bFGF (15 ng/ml) or angiopoietin (200 ng/ml) were applied and the cells were further cultured for 24 hours. The cells (floating and adherent) were collected and apoptotic cells were determined using cellular DNA fragmentation ELISA kit. Apoptosis rate of SFM and Ang-3 was found to be 100% and more than 140%, respectively. Hence, concluded that Ang-3 exhibited excellent apoptosis stimulating effect than SFM.

USE - For identifying angiopoietin activity, useful for **diagnosing** and treating **cancer** such as lung **cancer** (small cell lung **cancer**) and **breast cancer**, arthritis, diabetes, vascular disease such as atherosclerosis and restenosis associated with angioplasty or stent implantation and stroke/angioplasty (all claimed).

ADVANTAGE - The angiopoietin-3 (Ang-3) or nucleic acid molecule encoding Ang-3 effectively inhibits angiogenesis, spontaneous, metastasis or conversion from micrometastasis to macrometastasis (claimed). The Ang-3 enables to maintain health and integrity of functional blood vessels in adult tissues. The Ang-3 effectively promotes growth/survival of endothelial cells, and blocks proliferation of vascular smooth muscle cells.

Dwg.0/11

L7 ANSWER 3 OF 17 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2005490438 IN-PROCESS

DOCUMENT NUMBER: PubMed ID: 16011900

TITLE: Evaluation of leukocyte arylsulphatase a, serum interleukin-6 and urinary heparan sulphate following tamoxifen therapy in breast cancer.

AUTHOR: Oner-Iyidogan Yildiz; Oner Pernur; Kocak Hikmet; Lama Abdul; Gurdol Figen; Bekpinar Seldag; Unur Nurettin; Ozbek-Kir Zeynep

CORPORATE SOURCE: Istanbul University, Istanbul Faculty of Medicine, Department of Biochemistry, Capa, Istanbul 34093, Turkey.

SOURCE: Pharmacological research : the official journal of the Italian Pharmacological Society, (2005 Oct) Vol. 52,

No. 4, pp. 340-5.
Journal code: 8907422. ISSN: 1043-6618.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20050916
Last Updated on STN: 20051215

AB Leukocyte arylsulphatase A (AS-A) was shown to be significantly high in newly-**diagnosed breast cancer** patients. Previous reports imply a connection between serum interleukin-6 (IL-6) and breast cancer, possibly through a modulation of enzymes involved in estrogen synthesis. Abnormal distribution of **heparan sulphate proteoglycans** (**HSPGs**) in malignant breast epithelial cells suggests that they play a key role in the regulation of cell growth. Estradiol is believed to be effective in modulating glycosaminoglycans (GAGs) and their depolymerizing enzymes. Therefore, in this study, attempts were made to evaluate the activity of leukocyte arylsulphatase A, serum interleukin-6, urinary GAGs and heparan sulphate (HS) in response to tamoxifen (TAM) therapy in mastectomised breast cancer patients. Thirty-four patients (aged 30-82 years) were administered TAM (20 mg twice daily). Blood and urine samples of each patient were collected three times (at the beginning, and in third and sixth month of TAM therapy), and biochemical parameters were measured. There was no difference between baseline leukocyte AS-A activity and that measured after three months. At the end of six months, enzyme activity was significantly higher than the former values (p=0.022), but within the reference intervals reported in the literature. Although this increase might imply a normalization, the duration of TAM therapy is not long enough to make a decision about either regression or aggravation of the disease. TAM did not have any effect on serum IL-6, urinary HS and GAG levels which may be due to insensitivity of these variables to TAM during the short period of therapy. Both urinary GAG and HS levels measured at sixth month exhibited a positive correlation with the baseline level of leukocyte AS-A (p=0.005 and 0.009, respectively), suggesting that positive responses to the drug might be seen in patients with low AS-A activity.

L7 ANSWER 4 OF 17 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2005229364 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15817123
TITLE: Enhanced levels of Hsulf-1 interfere with heparin-binding growth factor signaling in pancreatic cancer.
AUTHOR: Li Junsheng; Kleeff Jorg; Abiatari Ivane; Kayed Hany; Giese Nathalia A; Felix Klaus; Giese Thomas; Buchler Markus W; Friess Helmut
CORPORATE SOURCE: Department of General Surgery, University of Heidelberg, Heidelberg, Germany.. lijunsheng70@hotmail.com
SOURCE: Molecular cancer [electronic resource], (2005 Apr 7) Vol. 4, No. 1, pp. 14. Electronic Publication: 2005-04-07.
Journal code: 101147698. E-ISSN: 1476-4598.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20050503
Last Updated on STN: 20051214

AB Hsulf-1 is a newly identified enzyme, which has the ability to decrease the growth of hepatocellular, ovarian, and head and neck squamous cell carcinoma cells by interfering with heparin-binding growth factor signaling. Since pancreatic cancers over-express a number of heparin-binding growth factors and their receptors, the expression and function of this enzyme in pancreatic cancer was analyzed. RESULTS: **Pancreatic cancer** samples expressed significantly (22.5-fold) increased Hsulf-1 mRNA levels compared to normal controls, and Hsulf-1 mRNA was localized in the cancer cells themselves as well as in peritumoral fibroblasts. 4 out of 8 examined **pancreatic cancer** cell lines expressed Hsulf-1, whereas its expression was below the level of **detection** in the other cell lines. Stable transfection of the Hsulf-1 negative Panc-1 pancreatic cancer cell line with a full length Hsulf-1 expression vector resulted in increased sulfatase activity and decreased cell-surface **heparan-sulfate proteoglycan** (**HSPG**) sulfation. Hsulf-1 expression reduced both anchorage-dependent and -independent cell growth and decreased FGF-2 mediated cell growth and invasion in this cell line. CONCLUSION: High expression of Hsulf-1 occurs in the stromal elements as well as in the tumor cells in pancreatic cancer and interferes with heparin-binding growth factor signaling.

L7 ANSWER 5 OF 17 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-784471 [77] WPIDS
DOC. NO. NON-CPI: N2004-618320
DOC. NO. CPI: C2004-274512
TITLE: **Diagnosing breast tumor**, by **detecting** expression product of one of 119 genes encoding, for example, ribosomal protein L27 and HIF-1 responsive RTP801, in **breast** tissue where increased expression indicates **neoplastic** state.
DERWENT CLASS: B04 D16 P31 S03
INVENTOR(S): MADDEN, S; SUKUMAR, S
PATENT ASSIGNEE(S): (MADD-I) MADDEN S; (SUKU-I) SUKUMAR S
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004091383	A2	20041028	(200477)*	EN	50
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
EP 1608255	A2	20051228	(200603)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PL PT RO SE SI SK TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004091383	A2	WO 2004-US9704	20040331
EP 1608255	A2	EP 2004-759056	20040331
		WO 2004-US9704	20040331

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1608255	A2 Based on	WO 2004091383

PRIORITY APPLN. INFO: US 2003-458960P 20030401

AN 2004-784471 [77] WPIDS

AB WO2004091383 A UPAB: 20041203

NOVELTY - Method (M1) to aid in **diagnosing breast tumor**, by **detecting** expression product of any one of 119 gene (such as hypothetical protein DKFZp434G171, HIF-1 responsive RTP801, ribosomal protein L27, cyclin-dependent kinase 3) in first **breast** tissue sample suspected of **neoplastic**, and comparing expression of gene in second **breast** tissue sample which is normal, where increased expression of gene in first sample indicates neoplastic state.

DETAILED DESCRIPTION - Method (M1) to aid in **diagnosing breast tumor**, involves **detecting** an expression product of at least any one of 119 gene in first **breast** tissue sample suspected of **neoplastic**, where the gene includes hypothetical protein DKFZp434G171, heat shock 70 kDa protein 1A, jagged 1 (Alagille syndrome), cyclin-dependent kinase 3, 6-phosphogluconolactonase, homolog of rat and mouse retinoid-inducible serine carboxypeptidase, plasmalemma vesicle associated protein, NADH:ubiquinone oxidoreductase MLRQ subunit homolog, HIF-1 responsive RTP801, ribosomal protein L27, etc. and comparing the expression of at least one gene in the first breast tissue sample with expression of at least one gene in the second breast tissue sample which is normal, where increased expression of at least one gene in the first breast tissue sample relative to the second tissue sample identifies the first **breast** tissue sample to be **neoplastic**.

INDEPENDENT CLAIMS are also included for the following:

(1) treating (M2) a breast tumor, involves contacting the cells of the breast tumor with an antibody that specifically binds to an extracellular epitope of a protein selected from benzodiazapine receptor (peripheral); cadherin 5, type 2, VE-cadherin (vascular epithelium), calcium channel, voltage-dependent, alpha 1H subunit; CD74 antigen (invariant polypeptide of major histocompatibility complex, class 1:1 antigen associated); CD9 antigen (p24); dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive), ectonucleoside triphosphate diphosphohydrolase 1, G protein-coupled receptor 4, hypothetical protein FLJ20898, hypoxia up-regulated 1, immediate early response 3, interferon, alpha-inducible protein (clone IFI-6-16), jagged 1 (Alagille syndrome), KLA,A0152 gene product, Lysosomal-associated multispanning membrane protein-5, major histocompatibility complex, class I, B, major histocompatibility complex, class I, C, NADH:ubiquinone oxidoreductase MLRQ subunit homolog, Notch homolog 3 (Drosophila), plasmalemma vesicle associated protein, solute carrier family 21 (prostaglandin transporter), member 2, TEMB, Thy-I cell surface antigen, receptor (calcitonin) activity modifying protein 3, sema domain, immunoglobulin domain (Ig), 43 benzodiazapine receptor (peripheral) - mitochondrial, and TEM17, where

immune destruction of cells of the breast tumor is triggered;

(2) identifying (M3) the test compound as potential anti-cancer or anti-breast tumor drug, involves contacting a test compound with a cell expressing at least one gene of (M1), monitoring an expressing product of the gene, and identifying the test compound as a potential anti-cancer drug if it decreases the expression of at least one gene; and

(3) inducing (M4) an immune response to a breast tumor, involves administering to a mammal a protein or nucleic acid encoding a protein of (M1), where an immune response to the protein is induced.

ACTIVITY - Cytostatic; Immunostimulant.

No supporting data is given.

MECHANISM OF ACTION - Immunotoxin; Radioimmunotherapeutic.

USE - (M1) is useful for **diagnosing breast tumor**. The tissue samples are isolated from same human. (M2) is useful for treating **breast tumor**. (M4) is useful for inducing an immune response to a **breast tumor** in a mammal. The mammal has a **breast tumor**. The mammal has a **breast tumor** that is surgically removed (all claimed).

ADVANTAGE - (M1) provides distinct **diagnosis** of **neoplastic** and normal endothelium in human **breast** at molecular level and has significant implication for the development of anti-angiogenic therapies.

Dwg.0/0

L7 ANSWER 6 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2004550014 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15522187

TITLE: Correlation of expression of heparanase to angiogenesis and prognosis of breast cancer.

AUTHOR: Liu Zhen-Zhen; Zhang Heng-Wei; Wei Bing; Cui Shu-De

CORPORATE SOURCE: Department of Breast, Henan Provincial Tumor Hospital, Zhengzhou, Henan 450 008, P.R. China.. liuzhenzhen@medmail.com.cn

SOURCE: Ai zheng = Aizheng = Chinese journal of cancer, (2004 Nov) Vol. 23, No. 11, pp. 1342-5. Journal code: 9424852. ISSN: 1000-467X.

PUB. COUNTRY: China

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Chinese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200512

ENTRY DATE: Entered STN: 20041104
Last Updated on STN: 20050122
Entered Medline: 20051209

AB BACKGROUND & OBJECTIVE: Heparanase is a **heparan sulfate proteoglycan** cleaving enzyme. It helps to degrade extracellular matrix and basement membrane, promote angiogenesis, and accelerate tumor metastasis. This study was to investigate correlation of heparanase expression to angiogenesis and prognosis of breast cancer. METHODS: Immunohistochemistry was used to **detect** heparanase and microvessel density (MVD) in 120 specimens of infiltrative ductal **breast cancer**, and 10 specimens of normal **breast** tissue. Correlation of heparanase expression to clinicopathologic factors and prognosis of breast cancer were analyzed using Chi-square test, t test, Kaplan-Meier method, and log-rank test. RESULTS: Positive rate of heparanase in breast cancer was 65% (78/120), significantly higher

than that in normal breast tissue (0, 0/10) (P< 0.05). MVD in breast cancer was 53.84+/-13.45, significantly higher than that in control group (33.32+/-8.55) (P< 0.01). Expression of heparanase positively correlated with tumor size, histological grade, lymph node metastasis, and clinical stage (P< 0.05) of breast cancer, and negatively correlated with 5-year survival rate (P< 0.05). MVD in heparanase positive group was much higher than that in heparanase negative group (P< 0.05), MVD positively correlated with heparanase expression (r=0.358,P< 0.01). CONCLUSION: Heparanase may promote angiogenesis, and may closely correlate with prognosis of breast cancer.

L7 ANSWER 7 OF 17 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-801219 [75] WPIDS
CROSS REFERENCE: 2000-339529 [29]
DOC. NO. NON-CPI: N2003-642048
DOC. NO. CPI: C2003-221187
TITLE: **Diagnostic** agent for treating human **breast cancer**, comprises a binding molecule that binds to **glypican-1** and a reporting molecule attached to binding molecule.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): KORC, M; LANDER, A D
PATENT ASSIGNEE(S): (KORC-I) KORC M; (LAND-I) LANDER A D
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003103980	A1	20030605	(200375)*		51

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003103980	A1 Provisional	US 1998-104510P	19981016
	Provisional	US 1999-121624P	19990225
	CIP of	WO 1999-US24176	19991015
	CIP of	US 2001-807575	20010413
	Provisional	US 2001-309722P	20010731
		US 2002-210327	20020731

PRIORITY APPLN. INFO: US 2002-210327 20020731; US 1998-104510P 19981016; US 1999-121624P 19990225; WO 1999-US24176 19991015; US 2001-807575 20010413; US 2001-309722P 20010731

AN 2003-801219 [75] WPIDS
CR 2000-339529 [29]
AB US2003103980 A UPAB: 20031120
NOVELTY - A **diagnostic** agent for human **breast cancer** comprises a binding molecule that binds to **glypican-1** and a reporting molecule attached to the binding molecule, is new. The **detection** of binding molecule indicates the presence of **breast cancer**.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) **diagnosing** human **breast cancer**,

which involves contacting a molecule that binds to **glypican-1** with either a body fluid or body tissue and **detecting** the molecule bound to **glypican-1** ; and

(2) treating human breast cancer, which involves administering the molecule that affects **glypican-1** by binding to extracellular region of **glypican-1**, cleaving an extracellular region of **glypican-1** and suppressing expression of **glypican-1**.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - None given.

USE - For treating breast cancer.

ADVANTAGE - The method enables effective treatment of breast cancer.

Dwg.0/30

L7 ANSWER 8 OF 17 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2003179126 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12697038

TITLE: Fibroblast growth factor 7, secreted by breast fibroblasts, is an interleukin-1beta-induced paracrine growth factor for human breast cells.

AUTHOR: Palmieri C; Roberts-Clark D; Assadi-Sabet A; Coope R C; O'Hare M; Sunters A; Hanby A; Slade M J; Gomm J J; Lam E W-F; Coombes R C

CORPORATE SOURCE: Cancer Research UK Laboratories, Department of Cancer Medicine, MRC Cyclotron Building, Imperial College, Hammersmith Hospital, Du Cane Road, London W12 0NN, UK.

SOURCE: The Journal of endocrinology, (2003 Apr) Vol. 177, No. 1, pp. 65-81.
Journal code: 0375363. ISSN: 0022-0795.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200306

ENTRY DATE: Entered STN: 20030417
Last Updated on STN: 20030625
Entered Medline: 20030624

AB Keratinocyte growth factor/fibroblast growth factor 7 (KGF/FGF7) is known to be a potent growth factor for mammary cells but its origin, cellular targets and mode of action in the breast are unclear. In this study, we carried out studies to determine the localisation of FGF7 and its receptor, and the related growth factor FGF10. We also **determined** the factors that regulate FGF7 release from stromal cells and the effects of FGF7 on normal and **neoplastic breast** cells. Using an FGF7-specific antibody which does not react with the FGF7 **heparan sulphate proteoglycan** (**HSPG**)-binding site, we showed epithelial and myoepithelial immunohistochemical staining in normal breast sections, and epithelial staining in breast carcinomas. Stromal staining was also detected in some lobular carcinomas as well as a subset of invasive ductal carcinomas. FGF10 and FGF receptor (FGFR)2 immunostaining showed a similar epithelial expression pattern, whereas no stromal staining was observed. We purified normal breast stromal, epithelial and myoepithelial cells and showed that FGF7 stimulated proliferation of both epithelial cell types, but not stromal fibroblasts. We also examined the effects of FGF7 on Matrigel-embedded organoids, containing both epithelial and

myoepithelial cells, and showed FGF7 induced an increase in cellular proliferation. Furthermore, conditioned medium derived from stromal cells was shown to increase the proliferation of normal and neoplastic breast epithelial cells, which could be abolished by a neutralising antibody to FGF7. Finally, we showed that interleukin-1beta, but not oestradiol or other oestrogen receptor ligands, caused a dose-related FGF7 release. Further results also indicate that the epithelial localisation of FGF7 and FGF10 in breast tissue sections is likely to be due to their binding to their cognate receptor. In summary, our findings suggest that FGF7 is a paracrine growth factor in the breast. FGF7 is produced by the breast stromal fibroblasts and has profound proliferative and morphogenic roles on both epithelial and myoepithelial cells.

L7 ANSWER 9 OF 17 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002060494 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11786412
TITLE: **Heparan sulfate proteoglycans** as regulators of fibroblast growth factor-2 receptor binding in breast carcinomas.
AUTHOR: Mundhenke Christoph; Meyer Kristy; Drew Sally; Friedl Andreas
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University of Wisconsin-Madison, Madison, Wisconsin 52792-8550, USA.
SOURCE: The American journal of pathology, (2002 Jan) Vol. 160, No. 1, pp. 185-94.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020707
Entered Medline: 20020705

AB Binding of fibroblast growth factors (FGFs) to their tyrosine kinase-signaling receptors (FGFRs) requires heparan sulfate (HS). HS proteoglycans (**HSPGs**) **determine** mitogenic responses of **breast carcinoma** cells to FGF-2 in vitro. For this study, we examined the role of **HSPGs** as modulators of FGF-2 binding to FGFR-1 in situ and in vitro. During stepwise reconstitution of the FGF-2/**HSPG**/FGFR-1 complex in situ, we identified an elevated ability of breast carcinoma cell **HSPGs** to promote receptor complex formation compared to normal breast epithelium. **HSPGs** isolated from the MCF-7 breast-carcinoma cell line were then fractionated according to their ability to assemble the FGF-2 receptor complex. All MCF-7 **HSPGs** are decorated with HS chains similarly capable of promoting FGF-2 receptor complex formation. In this in vitro model, syndecan-1 and syndecan-4 are the cell surface **HSPGs** contributing most to the complex formation. Relative expression levels of these syndecans in human **breast carcinoma** tissues correlate well with receptor complex formation in situ, indicating that in **breast carcinomas**, core protein levels **determine** FGF-2 receptor complex formation. However, variances in syndecan expression levels do not explain the difference in FGF-2 receptor complex formation between normal and malignant epithelial cells, suggesting that alterations in HS structure occur

during malignant transformation.

L7 ANSWER 10 OF 17 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001407894 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11454708
TITLE: **Glypican-1** is overexpressed in human breast cancer and modulates the mitogenic effects of multiple heparin-binding growth factors in breast cancer cells.
AUTHOR: Matsuda K; Maruyama H; Guo F; Kleeff J; Itakura J; Matsumoto Y; Lander A D; Korc M
CORPORATE SOURCE: Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Biological Chemistry, and Pharmacology, University of California, Irvine, California 92697, USA.
CONTRACT NUMBER: CA-40162 (NCI)
NS-26862 (NINDS)
SOURCE: Cancer research, (2001 Jul 15) Vol. 61, No. 14, pp. 5562-9.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB Glypicans are a family of glycosylphosphatidylinositol-anchored cell surface **heparan sulfate proteoglycans** implicated in the control of cellular growth and differentiation. Here we show that **glypican-1** is strongly expressed in human breast cancers, whereas expression of **glypican-1** is low in normal breast tissues. In contrast, the expression of glypican-3 and -4 is only slightly increased in **breast cancers** by comparison with normal **breast** tissues, and glypican-2 and -5 are below the level of **detection** by Northern blotting in both normal and cancer samples. Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with phosphoinositide-specific phospholipase-C abrogated the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor and fibroblast growth factor 2. Stable transfection of these cells with a **glypican-1** antisense construct markedly decreased **glypican-1** protein levels and the mitogenic response to the same heparin-binding growth factors, as well as that to heregulin alpha, heregulin beta, and hepatocyte growth factor. Syndecan-1 was also expressed at high levels in both breast cancer tissues and breast cancer cells when compared with normal breast tissues. There was a good correlation between **glypican-1** and syndecan-1 expression in the tumors. However, clones expressing the **glypican-1** antisense construct did not exhibit decreased syndecan-1 levels, indicating that loss of responsiveness to heparin-binding growth factors in these clones was not due to altered syndecan-1 expression. Furthermore, 8 of 10 tumors with stage 2 or 3 disease exhibited high levels of **glypican-1** by Northern blot analysis. In contrast, low levels of **glypican-1** mRNA were evident in 1 of 10 tumors with stage 2 or 3 disease and in 9 of 10 tumors with stage 1 disease. Taken together,

these data suggest that **glypican-1** may play a pivotal role in the ability of breast cancer cells to exhibit a mitogenic response to multiple heparin-binding growth factors and may contribute to disease progression in this malignancy.

L7 ANSWER 11 OF 17 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1999076030 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9858933
TITLE: Morphological aspects of altered basement membrane metabolism in invasive carcinomas of the breast and the larynx.
AUTHOR: Nerlich A G; Lebeau A; Hagedorn H G; Sauer U; Schleicher E D
CORPORATE SOURCE: Pathologisches Institut, Universitat Munchen, Germany.. Andreas.Nerlich@lrz.uni-muenchen.de
SOURCE: Anticancer research, (1998 Sep-Oct) Vol. 18, No. 5A, pp. 3515-20.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981229

AB In the present study we compared the localization of major basement membrane (BM) components and their mRNAs between invasive **carcinomas** of the **breast** (adenocarcinomas) and larynx **carcinomas** (squamous cell **carcinomas**, SCC), in order to **determine** the extent of BM production and deposition in malignant tumors of biologically different behaviour. Thus, breast carcinomas usually show a rapid locoregional/systemic spread, while the laryngeal SCCs normally show a more locally restricted growth pattern. While normal mammary glands and laryngeal mucosa revealed an intact epithelial BM as evidenced by a continuous linear staining for collagen IV, laminin-1, **heparan sulfate proteoglycan** (perlecan) and fibronectin-as well as collagen VII in the larynx mucosa-, this continuous staining was lost in the invasive carcinomas, however, affecting the two tumor types differently. In the breast carcinomas, a complete loss was seen even in well differentiated tumors affecting the various BM components similarly, while in the SCCs well differentiated carcinomas had retained significantly more BM material than poorly differentiated ones. In the SCCs, an "early" loss of collagen VII contrasted with a "later" loss of collagen IV, laminin, perlecan and fibronectin the extent of which was, however, associated with a decreasing degree of differentiation. In contrast to the protein findings, by use of the in-situ hybridization we observed a significant expression of mRNA for collagen IV, perlecan and fibronectin. The resulting pattern was comparable between both tumor types and not significantly related to the tumor cell differentiation. Both tumor cells and stroma cells were positively labelled with a more extensive labelling of the stroma cells. Our observations indicate a similar upregulation of the mRNAs for BM-components in breast and larynx carcinomas, but significant differences in the BM-protein deposition so that either major differences in presumed BM-proteolysis or further translational defects are suggested. Furthermore, it can be speculated that the far lesser amount of BM-material in the breast carcinomas may be linked to

the more aggressive metastatic spread of those tumors, particularly when compared to the SCCs.

L7 ANSWER 12 OF 17 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1998155651 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9494547
TITLE: Gene expression and protein deposition of major basement membrane components and TGF-beta 1 in human breast cancer.
AUTHOR: Nerlich A G; Wiest I; Wagner E; Sauer U; Schleicher E D
CORPORATE SOURCE: Pathologisches Institut, Universitat Munchen, Germany.. u7912ag@sunmail.lrz-muenchen.de
SOURCE: Anticancer research, (1997 Nov-Dec) Vol. 17, No. 6D, pp. 4443-9.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980326

AB In the present study we used immunohistochemistry and in-situ hybridization for the localization of major basement membrane (BM) components and their mRNA, respectively, in order to **determine** the extent of BM production and deposition in normal **mammary** tissue as well as in invasive mamma **carcinomas**. While normal mammary tissue showed an intact epithelial BM, as evidenced by a continuous linear staining for collagen i.v., laminin, **heparan sulfate proteoglycan** (perlecan) and fibronectin, this staining was widely lost in the invasive carcinomas. Non-invasive intraductal areas of the carcinomas (carcinoma-in-situ) revealed focal fragmentation and duplication of the epithelial BM. Using in-situ hybridization, we observed only focally positive mRNA-expression for collagen i.v.-, perlecan- and fibronectin-mRNA in normal glands, while mRNA-signals were significantly enhanced in one case of fibroadenoma and particularly in invasive and non-invasive carcinomas, regardless of the degree of tumor cell differentiation. In these instances both tumor and stroma cells were positively labelled. In addition, we could demonstrate a significant increase in the level of TGF-beta 1-mRNA--as the most active cytokine for the induction of matrix component production--by carcinoma cells and to lesser extent by stroma cells. The discrepancy between significantly enhanced mRNA-synthesis and loss in protein deposition points either to an upregulated activity of matrix degrading proteinases (matrix-metalloproteinases) or a posttranslational block of protein synthesis or both.

L7 ANSWER 13 OF 17 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:783945 SCISEARCH
THE GENUINE ARTICLE: YC284
TITLE: MCF-7 breast carcinoma cells overexpressing FGF-1 form vascularized, metastatic tumors in ovariectomized or tamoxifen-treated nude mice
AUTHOR: Zhang L R (Reprint); Kharbanda S; Chen D; Bullocks J; Miller D L; Ding I Y F; Hanfelt J; McLeskey S W; Kern F G

CORPORATE SOURCE: GEORGETOWN UNIV, MED CTR, SCH NURSING, WASHINGTON, DC 20007; GEORGETOWN UNIV, MED CTR, DEPT PHARMACOL, WASHINGTON, DC 20007; GEORGETOWN UNIV, MED CTR, DEPT MED, WASHINGTON, DC 20007; GEORGETOWN UNIV, MED CTR, DEPT BIOCHEM & MOL BIOL, WASHINGTON, DC 20007; GEORGETOWN UNIV, MED CTR, LOMBARDI CANC CTR, WASHINGTON, DC 20007
COUNTRY OF AUTHOR: USA
SOURCE: ONCOGENE, (23 OCT 1997) Vol. 15, No. 17, pp. 2093-2108

ISSN: 0950-9232.
PUBLISHER: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE, HAMPSHIRE, ENGLAND RG21 6XS.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 88
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB FGF-1 is expressed in a high proportion of **breast tumors**, While overexpression of FGF-4 in the MCF-7 **breast carcinoma** cell line confers the ability to form spontaneously metastasizing **tumors** in ovariectomized nude mice without estrogen supplementation and in mice that receive tamoxifen pellets, the response of a cell to individual FGFs can be controlled at multiple levels, and the significance of FGF-1 expression in human **breast tumors** is uncertain, To study the role of FGF-1, MCF-7 human **breast cancer carcinoma** cells, previously transfected with bacterial beta-galactosidase, were retransfected with FGF-1 expression vectors, FGF-1 transfectants formed large, vascularized tumors in ovariectomized nude mice without estrogen supplementation as web as in mice that received tamoxifen pellets, Lymphatic and pulmonary micrometastases were **detected** as deposits of X-gal-stained cells as early as 17 days after cell inoculation whereas no metastases were **detected** in estrogen-supplemented mice bearing similar-sized control tumors, When compared with controls, both clonal and polyclonal populations of FGF-1 overexpressing cells exhibited increased anchorage-independent growth and decreased population doubling times in estrogen-depleted or 4-hydroxytamoxifen containing medium, These results suggest that FGF signaling may be important in the transition of **breast cancer** cells from hormone-dependent to hormone-independent and from nonmetastatic to metastatic.

L7 ANSWER 14 OF 17 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:309658 SCISEARCH
THE GENUINE ARTICLE: HU107
TITLE: THE DISTRIBUTION OF FIBRONECTIN, LAMININ AND TETRANECTIN IN HUMAN BREAST-CANCER WITH SPECIAL ATTENTION TO THE EXTRACELLULAR-MATRIX
AUTHOR: CHRISTENSEN L (Reprint)
CORPORATE SOURCE: RIGSHOSP, DEPT PATHOL, DK-2100 COPENHAGEN, DENMARK (Reprint)
COUNTRY OF AUTHOR: DENMARK
SOURCE: APMIS, (1992) Vol. 100, Supp. [26], pp. 1-39.
ISSN: 0903-4641.

PUBLISHER: BLACKWELL MUNKSGAARD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 270
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Since Coman in 1944 observed that decreased adhesiveness is a characteristic of malignant cells and Grobstein 10 years later demonstrated that epithelial and mesenchymal cells influence each other when separated by a cell-impermeable filter, components of the extracellular matrix have been suspected of playing an active role in cancer growth. Breast cancer is frequently characterized by an increase in connective tissue fibroblastic cells and extracellular matrix, the nature and molecular composition of which is gradually being revealed. Two of the most studied and hence best known components of extracellular matrix are fibronectin and laminin. They are called adhesive or structural glycoproteins, because they are part of the stabilizing scaffold, which links connective tissue cells to each other (fibronectin) and connects connective tissues with parenchymatous cells via basement membranes (laminin). Both molecules harbour a variety of specific binding sites, which allow them to participate actively in basic dynamic processes such as cell modulation, -attachment, -spreading and -migration. Tetranectin is a recently discovered protein of human plasma and nucleated cells, which is suspected of participating in tissue degradation and proteolysis through its specific binding to plasminogen, a member of the plasminogen activation system.

The immunohistochemical studies of fibronectin, laminin and tetranectin, on which this thesis is based, were undertaken in order to investigate if qualitative or quantitative changes of these proteins between benign and malignant breast tissue would reflect the net effect of the different inherent characteristics of breast cancer cells known from experimental studies (i.e. unanchored growth, proteolysis, metastatic spread and de novo production of extracellular matrix components).

A significant increase in stromal fibronectin was a consistent finding in all infiltrating carcinomas, permitting the discrimination between such tumors and benign proliferative lesions as well as between carcinomas with a sarcomatoid appearance and true breast sarcomas. However, as a possible consequence of tumor heterogeneity this stromal reactivity pattern varied and tended to disappear focally along the invasive front of tumors with a high metastatic potential. A concurrent increase in the tumor cell expression of FN was found in poorly differentiated tumors, which could either be due to increased fibronectin production by the more anaplastic tumor cells or internalization of exogenous fibronectin bound to its receptor.

Whereas most of the extracellular fibronectin in breast cancer is thought to be produced by die stromal fibroblasts, extracellular laminin is considered a product of the epithelial tumor cells. It is therefore not surprising that laminin immunoreactivity within basement membranes was irregular already at the non invasive carcinoma stage and gradually disappeared with increasing anaplasia or metastatic potential of the tumor. The cellular expression of the protein was similar to the one described for fibronectin, but for laminin it has been shown by others that breast cancer cells possess increased numbers of laminin receptors with increasing anaplasia. It has further been suggested that attachment and traversion of vascular

basement membranes is facilitated by these cells if supplemented with laminin, because complexes of laminin and its receptor have been found to stimulate production of a basement membrane degrading enzyme, type IV collagenase, from the tumor cells.

Tetranectin was not detectable within the extracellular compartment of normal breast tissue, but it was produced by human embryonal lung fibroblasts in culture and incorporated into a pericellular matrix produced by the cells. Accordingly, tetranectin immunoreactivity occurred in the fibroblast-rich, proliferative connective tissue stroma of invasive breast carcinomas. Several studies have suggested that this proliferative response has an inhibitory effect on tumor growth and metastasis. Future studies will show if tetranectin plays an active role in this respect and will add to the rapidly growing information on the various components of the extracellular matrix and their specific interactions in neoplasia. This will undoubtedly improve the chances of finding new important tools for the **diagnosis**, prognosis and therapy of **breast cancer**.

L7 ANSWER 15 OF 17 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 91103684 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1702969
TITLE: [Monoclonal antibodies to the proteins of intermediate filaments and of basement membranes in the differential **diagnosis** of certain forms of human **breast tumors**].
Monoklonal'nye antitela k belkam promezhutochnykh filamentov i bazal'nykh membran v differentsial'noi diagnostike nekotorykh form opukholei molochnykh zhelez cheloveka.
AUTHOR: Gel'shtein V I; Chipysheva T A; Ermilova V D; Liubimov A V
SOURCE: Arkhiv patologii, (1990) Vol. 52, No. 9, pp. 12-8.
Journal code: 0370604. ISSN: 0004-1955.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 19960129
Entered Medline: 19910220

AB Monoclonal antibodies to keratins Number 8 and 17 specific for lining epithelium and myoepithelium of the mammary gland, respectively, as well as to basement membrane laminin, entactin, collagen type IV and **heparan sulfate proteoglycan** were used to the immunohistochemical analysis of 77 benign and malignant human breast lesions and that of 38 cases in which an intraoperative biopsy diagnosis was difficult. Morphologically similar benign and malignant proliferations were distinguished by keratin expression. In benign lesions both keratins were present, while in malignant ones only keratin Number 8 was expressed. Basement membranes associated with a myoepithelial layer were intact in benign lesions and in situ structures, but they were absent around the vast majority of invasive tumor foci. Basement membrane loss was important in differential diagnosis of benign sclerosing adenosis and cystadenopapilloma from invasive tubular and papillary carcinoma, respectively. Diagnosis of microinvasion in ductal and lobular carcinoma was much easier when combination of antibodies to keratins and basement membrane proteins

was used.

L7 ANSWER 16 OF 17 JICST-EPlus COPYRIGHT 2006 JST on STN
ACCESSION NUMBER: 870439736 JICST-EPlus
TITLE: Heterogeneity of the mesenchyme : Reappearance of fetal mesenchyme in adult.
AUTHOR: SAKAKURA TERUYO
CORPORATE SOURCE: Aichikenganse Ken
SOURCE: Connect Tissue, (1987) vol. 19, no. 1, pp. 71-74.
Journal Code: G0168B (Fig. 3, Ref. 7)
ISSN: 0916-572X
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Short Communication
LANGUAGE: Japanese
STATUS: New
AB In mammary gland development two mesenchymal tissues are distinguished. One is dense mammary mesenchyme immediately surrounding mammary epithelium and the other is fat pad precursor tissue which develops separately posterior to the mammary epithelium. The dense mammary mesenchyme synthesizes fibronectin and tenascin which is supposed to be important for the early morphogenesis of the mammary gland. The fat pad precursor tissue produces laminin and **proteo-heparan sulfate** to participate in typical mammary gland branching (J. Embryol. exp. Morph., 89 : 243, 1985). Thus, the mammary epithelium interacts with two different mesenchymes and undergoes mammary gland embryogenesis sequentially. Tenascin is a novel extracellular glycoprotein (Cell, 47 : 131, 1986) originally described as myotendinous antigen (J. Cell Biol., 98 : 1926, 1984). It consists of disulfide-linked subunits of 240kd and has a six-armed structure. In the present paper tenascin has been studied through the developmental history of the mammary gland development in mice using immunohistochemistry. Tenascin is **detected** in the dense mammary mesenchyme of fetal mammary rudiment but neither in the fat pad precursor tissue nor in the connective tissue of the normal adult **mammary** gland. It is interesting that, tenascin reappeared in malignant **mammary tumors**, but not in benign **tumors**.(author abst.)

L7 ANSWER 17 OF 17 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1985:363117 BIOSIS
DOCUMENT NUMBER: PREV198580033109; BA80:33109
TITLE: USEFULNESS OF BASEMENT MEMBRANE MARKERS IN TUMORAL PATHOLOGY.
AUTHOR(S): BIREMBAUT P [Reprint author]; CARON Y; ADNET J-J; FOIDART J-M
CORPORATE SOURCE: LAB POL BOUIN, HOPITAL MAISON BLANCHE, 45 RUE COGNACQ-JAY, 51 100 REIMS, FR
SOURCE: Journal of Pathology, (1985) Vol. 145, No. 4, pp. 283-296.
CODEN: JPTLAS. ISSN: 0022-3417.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The distribution of basement membrane (BM) markers, type IV collagen, laminin (LM), **heparan sulfate proteoglycan** (HSP) and fibronectin (FN) was studied by indirect immunofluorescence using specific antibodies, in [human] tumoral pathology. The disrupted pattern of BM by these markers in severe dysplastic lesions

of the breasts, the bronchi and uterine cervix provides evidence for malignancy. In invasive carcinomas, there is generally a loss of these BM components, with FN persisting in the stroma. The loss of these markers in BM is concomitant and superimposable in double staining studies. In embryonic tumors, the presence of BM markers is related to a mesenchymal differentiation of malignant cells with pericellular FN and/or maturation towards organoid structures with BM. In sarcomas, there is a loss of the pericellular BM staining around most transformed muscular and Schwann cells and adipocytes. The persistence of this labeling in some well-differentiated areas can help to diagnose the nature of the sarcoma. The persistence of intercellular filaments of FN corresponds to the mesenchymal and/or sarcomatous nature of undifferentiated anaplastic proliferations.

FILE 'CAPLUS' ENTERED AT 17:34:10 ON 16 MAR 2006
L8 131 SEA ABB=ON PLU=ON HS(W)(PROTEOGLYCAN OR PROTEO GLYCAN)
L9 1 SEA ABB=ON PLU=ON L8 AND (DIAGNOS? OR DETECT? OR DET## OR DETERM? OR SCREEN?)(S)((CANCER? OR CARCIN? OR TUMOUR OR TUMOR OR NEOPLAS?)(10A)(BREAST OR MAMMAR? OR PANCREAT? OR PANCREAS))
L10 0 SEA ABB=ON PLU=ON L9 NOT L5

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 17:36:07 ON 16 MAR 2006
L11 4 SEA ABB=ON PLU=ON L9
L12 0 SEA ABB=ON PLU=ON L11 NOT L6

(FILE 'CAPLUS' ENTERED AT 17:38:21 ON 16 MAR 2006)
L13 249 SEA ABB=ON PLU=ON (L2 OR L8)(S)ANTIBOD?
L14 3 SEA ABB=ON PLU=ON L13 AND (CANCER? OR CARCIN? OR TUMOUR OR TUMOR OR NEOPLAS?)(S)(PANCREAS OR PANCREAT? OR BREAST OR MAMMAR?)
L15 0 SEA ABB=ON PLU=ON L14 NOT L5

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 17:40:24 ON 16 MAR 2006
L16 27 SEA ABB=ON PLU=ON L14
L17 21 SEA ABB=ON PLU=ON L16 AND (DIAGNOS? OR DETECT? OR DET## OR DETERM? OR SCREEN?)
L18 11 SEA ABB=ON PLU=ON L17 NOT L6
L19 8 DUP REM L18 (3 DUPLICATES REMOVED)

L19 ANSWER 1 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-543535 [52] WPIDS
DOC. NO. CPI: C2004-199477
TITLE: **Screening** for inhibitors of glycosaminoglycan (GAG) interaction with effector cell adhesion molecules (ECAMs), useful for treating e.g., cancer, comprises contacting a GAG with an ECAM in the presence of a small organic compound.
DERWENT CLASS: B04 D16
INVENTOR(S): GREGOR, P; HARRIS, N; KOPPEL, J
PATENT ASSIGNEE(S): (RIMO-N) RIMONYX PHARM LTD
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004059278	A2	20040715	(200452)*	EN	60

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT
KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ
DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI
NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT
TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003288698 A1 20040722 (200476)
EP 1579214 A2 20050928 (200563) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU
LV MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004059278	A2	WO 2003-IL1116	20031230
AU 2003288698	A1	AU 2003-288698	20031230
EP 1579214	A2	EP 2003-780600	20031230
		WO 2003-IL1116	20031230

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003288698	A1 Based on	WO 2004059278
EP 1579214	A2 Based on	WO 2004059278

PRIORITY APPLN. INFO: IL 2002-153762 20021231
AN 2004-543535 [52] WPIDS
AB WO2004059278 A UPAB: 20040813
NOVELTY - **Screening** or identifying small organic compounds that inhibit the interaction of glycosaminoglycans (GAGs) with GAG specific effector cell adhesion molecules (ECAMs) comprises contacting a GAG with an ECAM in the presence of at least one small organic compound and measuring the amount of the GAG bound to the ECAM or the amount of the ECAM bound to the GAG.

DETAILED DESCRIPTION - **Screening** or identifying small organic compounds that inhibit the interaction of glycosaminoglycans (GAGs) with GAG specific effector cell adhesion molecules (ECAMs) comprises contacting a GAG with an ECAM in the presence of at least one small organic compound and measuring the amount of the GAG bound to the ECAM or the amount of the ECAM bound to the GAG.

A significant decrease in GAG-ECAM binding in the presence of the compound as compared to that without the compound identifies the compound as inhibitor compound inhibiting GAG-ECAM interaction.

INDEPENDENT CLAIMS are also included for the following:

(1) a compound identified according to the method above;

(2) a pharmaceutical composition comprising as an active ingredient an inhibitor compound capable of inhibiting the interaction of GAGs with GAG specific ECAMs, the compound identified by a **screening** method described above, further comprising a pharmaceutical diluent or carrier;

(3) a method for inhibiting cell adhesion or cell migration; and

(4) a method for modulating anticoagulant activity of GAGs in a subject.

ACTIVITY - Antiinflammatory; Immunosuppressive; Cytostatic; Antiarteriosclerotic; Antibacterial; Cardiovascular-Gen.; Vasotropic; Respiratory-Gen; Hepatotropic; Ophthalmological; Antiasthmatic;

Cerebroprotective; Nephrotropic; Dermatological; Antipsoriatic; Gastrointestinal-Gen.; Antiarthritic; Antirheumatic; Neuroprotective; Thyromimetic; Antithyroid; Muscular-Gen.; Antidiabetic; Osteopathic; Vulnerary.

MECHANISM OF ACTION - GAG Inhibitor.

Test drug was administered to Balb/c mice induced with acute edema. Results showed that the test compound significantly reduced carrageenan induced paw edema after intraperitoneal administration, thus displaying anti-inflammatory activity.

USE - A method of treatment comprising administering to a subject a pharmaceutical composition comprising as an active ingredient a small organic compound that inhibits the interaction of at least one GAG with at least one GAG specific ECAM, preventing cell adhesion or cell migration mediated by the GAG, is useful for treating or preventing a condition, process, or a disorder related to cell adhesion or migration in a subject.

The process, condition, or disorder related to cell adhesion or migration is inflammatory processes, autoimmune processes, **cancer, cancer** metastasis, atherosclerosis, or platelet-mediated pathologies. The inflammatory process is septic shock, wound associated sepsis, post-ischemic leukocyte-mediated tissue damage, reperfusion injury, frost-bite injury, shock, acute leukocyte-mediated lung injury, adult respiratory distress syndrome, acute **pancreatitis**, liver cirrhosis, uveitis, asthma, transplantation rejection, graft versus host disease, traumatic shock, stroke, traumatic brain injury, nephritis, acute and chronic inflammation, atopic dermatitis, psoriasis, or inflammatory bowel disease. The autoimmune process is rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, Hashimoto's thyroiditis, Grave's disease, Myasthenia gravis, insulin resistance, or autoimmune thrombocytopenic purpura. The **cancer** is leukemia. The disease related to cell adhesion or cell migration is bone degradation, restenosis, eczema, osteoporosis, and osteoarthritis or wound healing (all claimed).

The methods are useful for **screening** anti-inflammatory compounds useful for treating or **diagnosing** the above-defined diseases.

Dwg.0/11

L19 ANSWER 2 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-517671 [49] WPIDS
DOC. NO. CPI: C2004-191130
TITLE: Modulating the interaction between at least two different proteins by providing a compound capable of interfering with the receptor and the polypeptide interaction and presenting the compound to the different proteins.
DERWENT CLASS: B04 D16
INVENTOR(S): ALBRECHTSEN, M; BEREZIN, V; BOCK, E
PATENT ASSIGNEE(S): (ENKA-N) ENKAM PHARM AS
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004056865	A2	20040708	(200449)*	EN	154

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ

DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI
NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT
TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003287918 A1 20040714 (200474)
EP 1579218 A2 20050928 (200563) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU
LV MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004056865	A2	WO 2003-DK901	20031218
AU 2003287918	A1	AU 2003-287918	20031218
EP 1579218	A2	EP 2003-779758	20031218
		WO 2003-DK901	20031218

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003287918	A1 Based on	WO 2004056865
EP 1579218	A2 Based on	WO 2004056865

PRIORITY APPLN. INFO: DK 2003-330 20030303; DK 2002-1982 20021220

AN 2004-517671 [49] WPIDS

AB WO2004056865 A UPAB: 20040802

NOVELTY - Modulating the interaction between at least two different proteins by providing a compound capable of interfering with the receptor and the polypeptide interaction and presenting the compound to the different proteins, is new.

DETAILED DESCRIPTION - Modulating the interaction between at least two different proteins, where one of the proteins is represented by a functional cell-surface receptor, or its fragment or variant or by a polypeptide having a binding site to the receptor, where at least a part of the binding site comprises a sequence given in the specification comprises providing a compound capable of interacting with the receptor and/or polypeptide to interfere with the receptor and the polypeptide interaction and presenting the compound to the at least two different proteins.

INDEPENDENT CLAIMS are also included for:

(1) a **screening** method for a candidate compound capable of modulating the interaction between at least two different proteins;

(2) an assay for sequential **screening** of a candidate compound capable of modulating the interaction between at least two different proteins, where one of the least two different proteins is represented by a functional cell-surface receptor, and the other of the at least two different proteins is represented by a polypeptide having a binding site to the receptor;

(3) a method for molecular design for a compound capable of modulating the interaction between at least two different proteins, where one of the least two different proteins is represented by a functional cell-surface receptor, and the other of the at least two different proteins is represented by a polypeptide having a binding site to the receptor;

(4) a method for isolating a candidate compound capable of modulating the interaction between at least two different proteins;

(5) a peptide fragment;
(6) a compound comprising the peptide fragment;
(7) an **antibody** capable of binding to an epitope comprising a binding site to a cell surface receptor;
(8) a method for producing the **antibody** comprises administering to an animal the peptide fragment; and
(9) a method for producing a pharmaceutical composition.
ACTIVITY - Neuroprotective; Vulnerary; Antidiabetic; Nephrotropic.
No biological data given.
MECHANISM OF ACTION - Gene therapy.
USE - The method is useful in modulating the interaction between at least two different proteins, where one of the proteins is represented by a functional cell-surface receptor, or its fragment or variant or by a polypeptide having a binding site to the receptor, where at least a part of the binding site comprises a sequence given in the specification for preparing a composition for treating normal, degenerated or damaged NCAM presenting cells; solid **tumor** requiring neoangiogenesis; diseases and conditions of the central and peripheral nervous system, of the muscles or of various organs, e.g., postoperative nerve damage, traumatic nerve damage, impaired myelination of nerve fibers, post-ischemic damage, e.g. resulting from a stroke, Parkinson's disease, Alzheimer's disease, Huntington's disease, dementias such as multiinfarct dementia, sclerosis, nerve degeneration associated with diabetes mellitus, disorders affecting the circadian clock or neuro-muscular transmission, and schizophrenia, mood disorders, such as manic depression; diseases or conditions of the muscles including conditions with impaired function of neuro-muscular connections, such as after organ transplantation, or such as genetic or traumatic atrophic muscle disorders; degenerative conditions of the gonads, of the **pancreas** such as diabetes mellitus type I and II, of the kidney such as nephrosis or of the heart, liver and bowel; for preventing cell death of heart muscle cells, such as after acute myocardial infarction, or after angiogenesis; for promoting wound-healing; for revascularization; or for stimulating the ability to learn and/or the short and/or long-term memory (claimed).
Dwg.0/11

L19 ANSWER 3 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-290062 [28] WPIDS
DOC. NO. CPI: C2003-075385
TITLE: Evaluating the differentiation of totipotent, nearly totipotent, or pluripotent stem cells in response to chemical or biological agents, comprises exposing the cells to one or more putative differentiation inducing conditions.
DERWENT CLASS: B04 D16
INVENTOR(S): CHAPMAN, K; PAGE, R; SCHOLER, H; WEST, M D
PATENT ASSIGNEE(S): (ADCE-N) ADVANCED CELL TECHNOLOGY INC
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003018760	A2	20030306	(200328)*	EN	50

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE

DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM
PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ
VC VN YU ZA ZM ZW

US 2003224345 A1 20031204 (200380)
AU 2002324779 A1 20030310 (200452)
EP 1444326 A2 20040811 (200452) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV
MC MK NL PT RO SE SI SK TR
JP 2005500847 W 20050113 (200506) 148
MX 2004001725 A1 20050401 (200571)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003018760	A2	WO 2002-US26945	20020826
US 2003224345	A1 Provisional	US 2001-314316P	20010824
		US 2002-227282	20020826
AU 2002324779	A1	AU 2002-324779	20020826
EP 1444326	A2	EP 2002-759444	20020826
		WO 2002-US26945	20020826
JP 2005500847	W	WO 2002-US26945	20020826
		JP 2003-523611	20020826
MX 2004001725	A1	WO 2002-US26945	20020826
		MX 2004-1725	20040224

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002324779	A1 Based on	WO 2003018760
EP 1444326	A2 Based on	WO 2003018760
JP 2005500847	W Based on	WO 2003018760
MX 2004001725	A1 Based on	WO 2003018760

PRIORITY APPLN. INFO: US 2001-314316P 20010824; US 2002-227282 20020826

AN 2003-290062 [28] WPIDS

AB WO2003018760 A UPAB: 20030501

NOVELTY - Evaluating the differentiation of totipotent, nearly totipotent, or pluripotent stem cells, or cells from these cells, in response to one or more chemical or biological agents or physical conditions, comprising exposing the separate wells of cells to one or more putative differentiation inducing conditions simultaneously or sequentially, is new.

DETAILED DESCRIPTION - A method for evaluating the differentiation of totipotent, nearly totipotent, or pluripotent stem cells, or cells from these cells, in response to one or more chemical or biological agents or physical conditions, comprises:

(a) separating individual totipotent, nearly totipotent, or pluripotent stem cells, or cells from them or groups of such cells, in culture medium into one or several separate wells which may be open or closed, and which may be in the same or different apparatus;

(b) exposing the separate wells of cells to one or more putative differentiation inducing conditions simultaneously or sequentially; and

(c) **screening** the individual cells or groups of cells to **detect** markers of differentiation of the individual cells

or groups of cells.

INDEPENDENT CLAIMS are also included for the following:

(1) a library of two or more gene trap stem cell lines used simultaneously together to **screen** and **detect** agents or conditions that affect differentiation, survival, or proliferation of the stem cells;

(2) inducing differentiation of a stem cell to form cells of mesodermal lineage by exposing the stem cells to Flt-3;

(3) inducing differentiation of a stem cell to form cells of mesodermal and neural lineage by exposing the stem cells to TGFbeta-1;

(4) inducing differentiation of a stem cell to form cells selected from cells of endothelial lineage, and cells of endodermal lineage or appearance, comprising exposing the stem cells to tenascin;

(5) inducing differentiation of a stem cell comprising exposing the stem cells to Tie-1;

(6) inducing differentiation of a stem cell to form fibroblasts and/or other cells of connective tissue comprising exposing the stem cells to BMP-2;

(7) inducing differentiation of a stem cell to form myocardial cells lineage by exposing the stem cells to endothelial inducer cells; and

(8) inducing differentiation of a stem cell to form cells of mesodermal lineage comprising exposing the stem cells to fibroblast inducer cells.-

USE - The method is useful for identifying, analyzing and characterizing marker genes and gene products that specifically mark key regulatory steps associated with the induction of differentiation of stem cells into each of the important specific cell types. The method is also useful as a systematic, large-scale **screening** assay for identifying the combinations of biological, biochemical and physical agents or conditions that act simultaneously or sequentially to induce the differentiation of totipotent, nearly totipotent, or pluripotent stem cells into large number of different specific cell types, and for identifying treatments that may induce cancerous cells to undergo differentiation and inhibit their proliferation.

Dwg.0/21

L19 ANSWER 4 OF 8 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:33050 SCISEARCH

THE GENUINE ARTICLE: 756FC

TITLE: Inverse correlation between heparan sulfate composition and heparanase-1 gene expression in thyroid papillary carcinomas: A potential role in tumor metastasis

AUTHOR: Xu X L (Reprint); Quiros R M; Maxhimer J B; Jiang P; Marcinek R; Ain K B; Platt J L; Shen J K; Gattuso P; Prinz R A

CORPORATE SOURCE: Rush Univ, Med Ctr, Dept Gen Surg, 1653 W Congress Pkwy, Chicago, IL 60612 USA (Reprint); Rush Univ, Med Ctr, Dept Gen Surg, Chicago, IL 60612 USA; Rush Univ, Med Ctr, Dept Pathol, Chicago, IL 60612 USA; Univ Kentucky, Med Ctr, Thyroid Canc Res Lab, Dept Internal Med, Lexington, KY USA; Vet Affairs Med Ctr, Lexington, KY USA; Mayo Clin, Dept Surg, Rochester, MI USA; Mayo Clin, Dept Immunol, Rochester, MI USA; Mayo Clin, Dept Pediat, Rochester, MI USA

COUNTRY OF AUTHOR: USA

SOURCE: CLINICAL CANCER RESEARCH, (1 DEC 2003) Vol. 9, No. 16,

Part 1, pp. 5968-5979.
ISSN: 1078-0432.
PUBLISHER: AMER ASSOC CANCER RESEARCH, 615 CHESTNUT ST, 17TH FLOOR, PHILADELPHIA, PA 19106-4404 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 47
ENTRY DATE: Entered STN: 16 Jan 2004
Last Updated on STN: 16 Jan 2004

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose: Heparanase-1 (HPR1) is an endoglycosidase that degrades the side chains of heparan sulfate proteoglycan (HSPG), a key component in cell surfaces, the extracellular matrix (ECM), and the basement membrane (BM). The purpose of this study was to evaluate HPR1 expression in thyroid neoplasms and its effect in degrading the HSPG substrates in the ECM and BM and to **determine** its role in thyroid tumor metastasis.

Experimental Design: HPR1 mRNA expression was analyzed by using in situ hybridization with a digoxigenin-labeled antisense RNA probe on paraffin-embedded tumor sections and reverse transcription-PCR (RT-PCR) in fresh tumor tissues. HPR1 protein expression was analyzed by using immunohistochemical staining with an anti-HPR1 rabbit antiserum and immunofluorescence (IF) with an anti-HPR1 monoclonal antibody. The effect of HPR1 expression in thyroid neoplasms was analyzed by examining the presence and integrity of the **HSPG** substrates in the ECM and BM using IF staining with a specific monoclonal **antibody** against heparan sulfate. The relationship of HPR1 expression in papillary thyroid carcinomas (PTCs) with various clincopathological parameters was analyzed statistically. The role of HPR1 in thyroid tumor metastasis was further examined by comparing HPR1 levels in 10 thyroid tumor cell lines to their invasive and metastatic potential.

Results: In situ hybridization analysis of 81 tumor samples (62 papillary carcinomas and 19 follicular adenomas) revealed that HPR1 was expressed at a much higher frequency in PTCs than in follicular adenomas ($P < 0.05$). RT-PCR analyses of fresh tumor tissues revealed that HPR1 mRNA could be **detected** in primary and metastatic thyroid papillary carcinomas. HPR1 expression was confirmed at the protein level by immunohistochemical staining and IF stainings. IF analysis of HSPG revealed that HS was deposited abundantly in the BM of normal thyroid follicles and benign follicular adenomas but was absent in most thyroid papillary carcinomas. A lack of heparan sulfate in PTCs inversely correlated with HPR1 expression. Clinicopathological data analyses revealed that PTCs with local and distant metastases scored HPR1 positive at a significantly higher frequency than nonmetastatic thyroid cancers ($P = 0.02$). To further explore the role of HPR1 in tumor metastases, we characterized HPR1 expression in 10 thyroid tumor cell lines using RT-PCR and Western blot and measured HPR1 enzymatic activity using a novel ELISA. HPR1 was differentially expressed in different types of cell lines; overexpression of HPR1 in two tumor cell lines led to a dramatic increase of their invasive potential in vitro in an artificial BM.

Conclusions: Our study suggests that HPR1 expressed in papillary carcinomas is functional and that HPR1 expression is associated with thyroid tumor malignancy and may significantly contribute to thyroid tumor metastases.

L19 ANSWER 5 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-339529 [29] WPIDS

CROSS REFERENCE: 2003-801219 [75]
DOC. NO. NON-CPI: N2000-254919
DOC. NO. CPI: C2000-102999
TITLE: **Diagnostic** agent for human cancer, **detects** overexpression of **glypican-1** or syndecan-1, also therapeutic composition containing agent that affects **glypican-1**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): KORC, M; LANDER, A
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 88
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000023109	A1	20000427	(200029)*	EN	83
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 2000011181	A	20000508	(200037)		
EP 1146903	A1	20011024	(200171)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 769125	B	20040115	(200409)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000023109	A1	WO 1999-US24176	19991015
AU 2000011181	A	AU 2000-11181	19991015
EP 1146903	A1	EP 1999-954963	19991015
		WO 1999-US24176	19991015
AU 769125	B	AU 2000-11181	19991015

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000011181	A	Based on	WO 2000023109
EP 1146903	A1	Based on	WO 2000023109
AU 769125	B	Previous Publ.	AU 2000011181
		Based on	WO 2000023109

PRIORITY APPLN. INFO: US 1999-121624P 19990225; US 1998-104510P 19981016
AN 2000-339529 [29] WPIDS
CR 2003-801219 [75]
AB WO 200023109 A UPAB: 20040205
NOVELTY - **Diagnostic** agent (A) for human cancer comprises a molecule (I) that binds to **glypican-1** (G1) or syndecan-1 (S1) and a reporter (II) attached to (I) so that presence of (I) can be **detected** from (II).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) therapeutic agent for slowing growth of human cancer cells comprising a molecule (III) that affects G1 by binding to its extracellular region (ECR) or cleaves ECR or suppresses expression of ECR;

(b) **diagnosing** human cancer by reacting a body fluid sample with (I) and **detecting** binding; and

(c) slowing growth of human cancer cells by administering (III).

ACTIVITY - Anticancer.

1 million PANC-1 (**pancreatic cancer**) cells sham transfected (a1) or transfected with G1-specific antisense mRNA (b1) were injected subcutaneously into athymic mice. Initially there was little difference in the **tumor** growth rates but after 8 weeks the **tumor** volume in (b1) was only about 1/3 of that in (a1).

MECHANISM OF ACTION - Expression of G1 (also of S1 in **breast cancer**) is upregulated in human **cancers** (specifically of **breast** and **pancreas**). G1 is essential for the mitogenic activities of fibroblast growth factor, HB-EGF (heparin-binding epidermal growth factor-like growth factor) and hepatocyte growth factor. Reducing its expression will thus reduce the mitogenic response and hence tumorigenicity.

USE - (I) is used to **detect** G1 and S1 in a body fluid or to image them in tissues, specifically for **diagnosis** of cancer. Agents that affect G1 and S1 are useful for treating cancer.

DESCRIPTION OF DRAWING(S) - Results of Northern blotting for **glypican-1** in **pancreatic** tissues, showing overexpression in **cancers** relative to normal or chronic **pancreatitis** tissues.

Dwg.0/26

L19 ANSWER 6 OF 8 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER:	93146648 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 8425764
TITLE:	Myoepithelial and basement membrane antigens in benign and malignant human **breast tumors**.
AUTHOR:	Guelstein V I; Tchypysheva T A; Ermilova V D; Ljubimov A V
CORPORATE SOURCE:	Cancer Research Center, Russian Academy of Medical Sciences, Moscow.
SOURCE:	International journal of cancer. Journal international du cancer, (1993 Jan 21) Vol. 53, No. 2, pp. 269-77. Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199303
ENTRY DATE:	Entered STN: 19930312 Last Updated on STN: 19930312 Entered Medline: 19930304

AB Serial cryostat sections of 160 human breast lesions and of 9 lymph-node metastases were studied by indirect immunofluorescence. We used monoclonal **antibodies** (MAbs) to lining-epithelium-specific keratin 8 and to myoepithelium-specific keratin 17 in combination with polyclonal and monoclonal **antibodies** to major basement membrane components, laminin, collagen type IV, entactin/nidogen, and large **heparan sulfate proteoglycan** (perlecan) core protein. Continuous basement membranes adjacent to a basal layer of keratin-17-positive

myoepithelial cells were typical for normal, benign and in situ carcinomatous structures. In invasive and metastatic structures, always formed by keratin-8-positive tumor cells, basement membranes were found only rarely and with conspicuous fragmentations. This lack of basement membranes correlated with loss of myoepithelium identified by staining for keratin 17. In comedo structures of invasive ductal carcinomas and in papillary carcinomas, fibrovascular complexes with numerous blood vessels and deposition of basement membrane material were often seen in the stroma. Immunomorphological analysis of 41 cases of doubtful **diagnosis** at intra-operative biopsy was also performed. A combination of MAbs to keratins 8 and 17, and to basement membrane components, made it possible to distinguish between morphologically similar benign and malignant proliferations and to **detect** single-cell invasion of the stroma. This combination of antibodies may be recommended as an auxiliary immunomorphological tool for differential **diagnosis** of intra-operative breast biopsies in dubious cases.

L19 ANSWER 7 OF 8 MEDLINE on STN
ACCESSION NUMBER: 85210310 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2987468
TITLE: Usefulness of basement membrane markers in tumoural pathology.
AUTHOR: Birembaut P; Caron Y; Adnet J J; Foidart J M
SOURCE: The Journal of pathology, (1985 Apr) Vol. 145, No. 4, pp. 283-96.
Journal code: 0204634. ISSN: 0022-3417.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198507
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850708

AB The distribution of basement membrane (BM) markers, type IV collagen, laminin (LM), **heparan sulphate proteoglycan** (HSP) and fibronectin (FN) has been studied by indirect immunofluorescence using specific **antibodies**, in tumoural pathology. The disrupted pattern of BM by these markers in severe dysplastic lesions of the breasts, the bronchi and uterine cervix provides evidence for malignancy. In invasive carcinomas, there is generally a loss of these BM components, with FN persisting in the stroma. The loss of these markers in BM is concomitant and superimposable in double staining studies. In embryonic tumours, the presence of BM markers is related to a mesenchymal differentiation of malignant cells with pericellular FN and/or maturation towards organoid structures with BM. In sarcomas, there is a loss of the pericellular BM staining around most transformed muscular and Schwann cells and adipocytes. The persistence of this labelling in some well-differentiated areas can help to **diagnose** the nature of the sarcoma. The persistence of intercellular filaments of FN corresponds to the mesenchymal and/or sarcomatous nature of undifferentiated anaplastic proliferations.

L19 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 85123285 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6395922
TITLE: [Basement membranes and tumor pathology].

Searcher : Shears 571-272-2528

Membranes basales et pathologie tumorale.
AUTHOR: Birembaut P; Caron Y; Loiseaux F; Adnet J J
SOURCE: Bulletin du cancer, (1984) Vol. 71, No. 5, pp. 468-73.
Journal code: 0072416. ISSN: 0007-4551.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198504
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19980206
Entered Medline: 19850404

AB The distribution of four basement membrane components, type IV collagen (C IV), laminin (LM), **heparan sulfate proteoglycan** (HSP) and fibronection (FN) has been studied by indirect immunofluorescence using specific **antibodies**, in benign and malignant proliferations of the **mammary** gland and in soft tissue **tumors**. In **breast carcinomas**, specially intraductal **cancers**, there is a progressive and concomitant loss of these macromolecules around tumoral cells, preceding an overt tumoral invasion. In sarcomas, FN is frequently seen between malignant cells but the regular pericellular labeling observed around normal muscular cells, Schwann cells and adipocytes is absent. Nevertheless, the persistance of some pericellular staining with anti-C IV, anti-LM, anti-HSP and anti-FN antisera, in most differentiated territories of liposarcomas, leiomyosarcomas and neurifibrosarcomas can help to the **diagnosis** of such lesions.

FILE 'MEDLINE' ENTERED AT 17:43:30 ON 16 MAR 2006

FILE LAST UPDATED: 16 MAR 2006 (20060316/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L20	1871	SEA FILE=MEDLINE	ABB=ON	PLU=ON	"HEPARAN SULFATE PROTEOGLY CAN"/CT
L21	32072	SEA FILE=MEDLINE	ABB=ON	PLU=ON	"PANCREATIC NEOPLASMS"/CT
L22	131008	SEA FILE=MEDLINE	ABB=ON	PLU=ON	"BREAST NEOPLASMS"/CT
L23	22	SEA FILE=MEDLINE	ABB=ON	PLU=ON	L20 AND (L21 OR L22)
L24	0	SEA FILE=MEDLINE	ABB=ON	PLU=ON	L23 AND (DIAGNOSIS OR

DIAGNOSTIC USE)/CT

L23 ANSWER 1 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2004562241 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15533755
TITLE: Heparan sulfate proteoglycans and heparanase--partners in osteolytic tumor growth and metastasis.
AUTHOR: Sanderson Ralph D; Yang Yang; Suva Larry J; Kelly Thomas
CORPORATE SOURCE: Department of Pathology and Arkansas Cancer Research Center, University of Arkansas, for Medical Sciences, Little Rock, AR, USA.. RDSanderson@uams.edu
CONTRACT NUMBER: CA103054 (NCI)
CA68494 (NCI)
SOURCE: Matrix biology : journal of the International Society for Matrix Biology, (2004 Oct) Vol. 23, No. 6, pp. 341-52. Ref: 140
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041110
Last Updated on STN: 20050409
Entered Medline: 20050408
ED Entered STN: 20041110
Last Updated on STN: 20050409
Entered Medline: 20050408
AB This review summarizes a series of studies demonstrating that heparan sulfate proteoglycans act to promote the growth and metastasis of myeloma and breast tumors, two tumors that home to, and grow within, bone. Much of the growth-promoting effect of proteoglycans in these tumors may reside in the shed form of syndecan-1 that acts to favorably condition the tumor microenvironment. Moreover, the interplay between heparan sulfate and the extracellular enzyme heparanase-1 also has important regulatory implications. Recent studies indicate that the activity of heparanase, which likely releases heparin sulfate-bound growth factors and generates highly active heparan sulfate fragments, also promotes growth and metastasis of myeloma and breast tumors. Understanding the role of heparan sulfate and heparanase in the regulation of tumor behavior may lead to new therapeutic approaches for treating cancer.

L23 ANSWER 2 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2004506173 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15292202
TITLE: Heparanase uptake is mediated by cell membrane heparan sulfate proteoglycans.
AUTHOR: Gingis-Velitski Svetlana; Zetser Anna; Kaplan Victoria; Ben-Zaken Olga; Cohen Esti; Levy-Adam Flonia; Bashenko Yulia; Flugelman Moshe Y; Vlodavsky Israel; Ilan Neta
CORPORATE SOURCE: Cancer and Vascular Biology Research Center, Bruce Rappaport Faculty of Medicine, Technion, Haifa 31096, Israel.
CONTRACT NUMBER: R01 CA106456-01 (NCI)
SOURCE: The Journal of biological chemistry, (2004 Oct 15) Vol. 279, No. 42, pp. 44084-92. Electronic Publication:

2004-07-29.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041013
Last Updated on STN: 20041220
Entered Medline: 20041214
ED Entered STN: 20041013
Last Updated on STN: 20041220
Entered Medline: 20041214
AB Heparanase is a mammalian endoglycosidase that degrades heparan sulfate (HS) at specific intrachain sites, an activity that is strongly implicated in cell dissemination associated with metastasis and inflammation. In addition to its structural role in extracellular matrix assembly and integrity, HS sequesters a multitude of polypeptides that reside in the extracellular matrix as a reservoir. A variety of growth factors, cytokines, chemokines, and enzymes can be released by heparanase activity and profoundly affect cell and tissue function. Thus, heparanase bioavailability, accessibility, and activity should be kept tightly regulated. We provide evidence that HS is not only a substrate for, but also a regulator of, heparanase. Addition of heparin or xylosides to cell cultures resulted in a pronounced accumulation of, heparanase in the culture medium, whereas sodium chlorate had no such effect. Moreover, cellular uptake of heparanase was markedly reduced in HS-deficient CHO-745 mutant cells, heparan sulfate proteoglycan-deficient HT-29 colon cancer cells, and heparinase-treated cells. We also studied the heparanase biosynthetic route and found that the half-life of the active enzyme is approximately 30 h. This and previous localization studies suggest that heparanase resides in the endosomal/lysosomal compartment for a relatively long period of time and is likely to play a role in the normal turnover of HS. Co-localization studies and cell fractionation following heparanase addition have identified syndecan family members as candidate molecules responsible for heparanase uptake, providing an efficient mechanism that limits extracellular accumulation and function of heparanase.

L23 ANSWER 3 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2004346086 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15249209
TITLE: Glypican-1 antisense transfection modulates TGF-beta-dependent signaling in Colo-357 pancreatic cancer cells.
AUTHOR: Li Junsheng; Kleeff Jorg; Kayed Hany; Felix Klaus; Penzel Roland; Buchler Markus W; Korc Murray; Friess Helmut
CORPORATE SOURCE: Department of General Surgery, University of Heidelberg, Heidelberg, Germany.
CONTRACT NUMBER: CA-10130 (NCI)
CA-75059 (NCI)
SOURCE: Biochemical and biophysical research communications, (2004 Aug 6) Vol. 320, No. 4, pp. 1148-55.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

Searcher : Shears 571-272-2528

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040714
Last Updated on STN: 20040911
Entered Medline: 20040910

ED Entered STN: 20040714
Last Updated on STN: 20040911
Entered Medline: 20040910

AB The heparan sulfate proteoglycan glypican-1 is essential as a co-receptor for heparin binding growth factors, such as HB-EGF and FGF-2, in pancreatic cancer cells. In the present study, the role of glypican-1 in the regulation of TGF-beta signaling was investigated. Colo-357 pancreatic cancer cells were stably transfected with a full-length glypican-1 antisense construct. Cell growth was determined by MTT and soft agar assays. TGF-beta1 induced p21 expression and Smad2 phosphorylation were analyzed by immunoblotting. PAI-1 promoter activity was determined by luciferase assays. Down-regulation of glypican-1 expression by stable transfection of a full-length glypican-1 antisense construct resulted in decreased anchorage-dependent and -independent cell growth in Colo-357 pancreatic cancer cells and attenuated TGF-beta1 induced cell growth inhibition, Smad2 phosphorylation, and PAI-1 promoter activity. There was, however, no significant difference in TGF-beta1 induced p21 expression and Smad2 nuclear translocation. In conclusion, glypican-1 is required for efficient TGF-beta1 signaling in pancreatic cancer cells.

L23 ANSWER 4 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2004292489 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15194227
TITLE: IGF-I affects glycosaminoglycan/proteoglycan synthesis in breast cancer cells through tyrosine kinase-dependent and -independent pathways.
AUTHOR: Mitropoulou Theoni N; Theocharis Achilleas D; Nikitovic Dragana; Karamanos Nikos K; Tzanakakis George N
CORPORATE SOURCE: Section of Organic Chemistry, Biochemistry and Natural Products, Laboratory of Biochemistry, Department of Chemistry, University of Patras, 26110 Patras, Greece.
SOURCE: Biochimie, (2004 Apr-May) Vol. 86, No. 4-5, pp. 251-9. Journal code: 1264604. ISSN: 0300-9084.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20040615
Last Updated on STN: 20050114
Entered Medline: 20050113

ED Entered STN: 20040615
Last Updated on STN: 20050114
Entered Medline: 20050113

AB The insulin-like growth factor I (IGF-I) has been implicated in breast cancer development acting through insulin-like growth factor I receptor (IGF-IR), but also through estrogen receptor (ER). The effect of IGF on proteoglycan (PG) synthesis by two human breast cancer epithelial cell lines, the ER-positive MCF-7 and the ER-negative BT-20, was studied alone and in combination with genistein. Both cell lines synthesise hyaluronan (HA), matrix secreted and cell membrane-associated galactosaminoglycan containing

proteoglycans (GalAGPGs) and heparan sulphate proteoglycans (HSPGs) in variable amounts. IGF-I affects the synthesis of PGs by BT-20 cells by decreasing the amounts of HA and secreted GalAGPGs and HSPGs and upregulates the expression of cell membrane-associated GalAGPGs and HSPGs. IGF-I exerts this effect on BT-20 cells acting mainly through receptors with protein tyrosine kinase activity (PTK). In contrast, IGF-I stimulates the synthesis of secreted GalAGPGs and HSPGs by MCF-7 cells, exhibiting only a slight suppression on synthesis of cell-associated GalAGPGs and HSPGs. The regulatory effect of IGF-I on PGs distribution in MCF-7 cells is mediated through a mix of pathways, which involves both receptors with PTK activity and PTK-independent signalling. It is suggested that the effects of IGF-I on the synthesis and distribution of PGs by epithelial breast cancer cells also depend on the presence or the absence of ER. The result of the IGF-I action is the balanced biosynthesis between the matrix and cell-associated PGs in both cell lines, approaching a common biosynthetic phenotype.

L23 ANSWER 5 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2004072687 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14717698
TITLE: Surface nucleolin participates in both the binding and endocytosis of lactoferrin in target cells.
AUTHOR: Legrand Dominique; Vigie Keveen; Said Elias A; Elass Elisabeth; Masson Maryse; Slomianny Marie-Christine; Carpentier Mathieu; Briand Jean-Paul; Mazurier Joel; Hovanessian Ara G
CORPORATE SOURCE: Institut Federatif de Recherche n degrees 118, Universite des Sciences et Technologies de Lille, Villeneuve d'Ascq, France.. dominique.legrand@univ-lille1.fr
SOURCE: European journal of biochemistry / FEBS, (2004 Jan) Vol. 271, No. 2, pp. 303-17.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040214
Last Updated on STN: 20040303
Entered Medline: 20040302

ED Entered STN: 20040214
Last Updated on STN: 20040303
Entered Medline: 20040302

AB Lactoferrin (Lf), a multifunctional molecule present in mammalian secretions and blood, plays important roles in host defense and cancer. Indeed, Lf has been reported to inhibit the proliferation of cancerous mammary gland epithelial cells and manifest a potent antiviral activity against human immunodeficiency virus and human cytomegalovirus. The Lf-binding sites on the cell surface appear to be proteoglycans and other as yet undefined protein(s). Here, we isolated a Lf-binding 105 kDa molecular mass protein from cell extracts and identified it as human nucleolin. Medium-affinity interactions (approximately 240 nm) between Lf and purified nucleolin were further illustrated by surface plasmon resonance assays. The interaction of Lf with the cell surface-expressed nucleolin was then demonstrated through competitive binding studies between Lf and the anti-human immunodeficiency virus pseudopeptide, HB-19, which binds

specifically surface-expressed nucleolin independently of proteoglycans. Interestingly, binding competition studies between HB-19 and various Lf derivatives in proteoglycan-deficient hamster cells suggested that the nucleolin-binding site is located in both the N- and C-terminal lobes of Lf, whereas the basic N-terminal region is dispensable. On intact cells, Lf co-localizes with surface nucleolin and together they become internalized through vesicles of the recycling/degradation pathway by an active process. Morever, a small proportion of Lf appears to translocate in the nucleus of cells. Finally, the observations that endocytosis of Lf is inhibited by the HB-19 pseudopeptide, and the lack of Lf endocytosis in proteoglycan-deficient cells despite Lf binding, point out that both nucleolin and proteoglycans are implicated in the mechanism of Lf endocytosis.

L23 ANSWER 6 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2002106892 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11823498
TITLE: Obligatory requirement of sulfation for P-selectin binding to human salivary gland carcinoma Acc-M cells and breast carcinoma ZR-75-30 cells.
AUTHOR: Ma Yan-Qing; Geng Jian-Guo
CORPORATE SOURCE: Laboratory of Molecular Cell Biology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2002 Feb 15) Vol. 168, No. 4, pp. 1690-6.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020213
Last Updated on STN: 20020305
Entered Medline: 20020304

ED Entered STN: 20020213
Last Updated on STN: 20020305
Entered Medline: 20020304

AB Stimulated endothelial cells and activated platelets express P-selectin, which reacts with P-selectin glycoprotein ligand-1 (PSGL-1) for leukocyte rolling on the stimulated endothelial cells and heterotypic aggregation of the activated platelets on leukocytes. P-selectin also binds to several cancer cells in vitro and promotes the growth and metastasis of human colon carcinoma in vivo. The P-selectin/PSGL-1 interaction requires tyrosine sulfation. However, it is unknown whether sulfation is necessary for P-selectin binding to somatic cancer cells. In this study, we show that P-selectin mediated adhesion of Acc-M cells, a cell line derived from a human adenoid cystic carcinoma of salivary gland. These cells had a moderate expression of heparan sulfate-like proteoglycans, but had no detectable expressions of PSGL-1, CD24, Lewis(x), and sialyl Lewis(x). Treatment with sodium chlorate (a sulfation biosynthesis inhibitor), but not 4-methylumbelliferyl-beta-D-xyloside (a proteoglycan biosynthesis inhibitor) or heparinases, reduced adhesion of these cells to P-selectin. Sodium chlorate also inhibited the P-selectin precipitation of the 160-, 54-, and 36-kDa molecules from the cell surface of Acc-M cells. Furthermore, P-selectin could bind to human

breast carcinoma ZR-75-30 cells in a sulfation-dependent manner. Our results thus indicate that sulfation is essential for adhesion of nonblood-borne, epithelial-like human cancer cells to P-selectin.

L23 ANSWER 7 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2002060494 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11786412
TITLE: Heparan sulfate proteoglycans as regulators of fibroblast growth factor-2 receptor binding in breast carcinomas.
AUTHOR: Mundhenke Christoph; Meyer Kristy; Drew Sally; Friedl Andreas
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University of Wisconsin-Madison, Madison, Wisconsin 52792-8550, USA.
SOURCE: The American journal of pathology, (2002 Jan) Vol. 160, No. 1, pp. 185-94.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020707
Entered Medline: 20020705
ED Entered STN: 20020125
Last Updated on STN: 20020707
Entered Medline: 20020705
AB Binding of fibroblast growth factors (FGFs) to their tyrosine kinase-signaling receptors (FGFRs) requires heparan sulfate (HS). HS proteoglycans (HSPGs) determine mitogenic responses of breast carcinoma cells to FGF-2 in vitro. For this study, we examined the role of HSPGs as modulators of FGF-2 binding to FGFR-1 in situ and in vitro. During stepwise reconstitution of the FGF-2/HSPG/FGFR-1 complex in situ, we identified an elevated ability of breast carcinoma cell HSPGs to promote receptor complex formation compared to normal breast epithelium. HSPGs isolated from the MCF-7 breast-carcinoma cell line were then fractionated according to their ability to assemble the FGF-2 receptor complex. All MCF-7 HSPGs are decorated with HS chains similarly capable of promoting FGF-2 receptor complex formation. In this in vitro model, syndecan-1 and syndecan-4 are the cell surface HSPGs contributing most to the complex formation. Relative expression levels of these syndecans in human breast carcinoma tissues correlate well with receptor complex formation in situ, indicating that in breast carcinomas, core protein levels determine FGF-2 receptor complex formation. However, variances in syndecan expression levels do not explain the difference in FGF-2 receptor complex formation between normal and malignant epithelial cells, suggesting that alterations in HS structure occur during malignant transformation.

L23 ANSWER 8 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2001649944 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11704870
TITLE: Glypican-3 expression is silenced in human breast cancer.
AUTHOR: Xiang Y Y; Ladeda V; Filmus J
CORPORATE SOURCE: Sunnybrook and Women's College Health Sciences Centre,

Molecular and Cell Biology Research Program, 2075 Bayview Avenue, Toronto, Ontario, M4N 3M5, Canada.
SOURCE: Oncogene, (2001 Nov 1) Vol. 20, No. 50, pp. 7408-12.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011113
Last Updated on STN: 20020123
Entered Medline: 20011213
ED Entered STN: 20011113
Last Updated on STN: 20020123
Entered Medline: 20011213
AB Glypican-3 (GPC3) is a membrane-bound heparan sulfate proteoglycan that is mutated in the Simpson-Golabi-Behmel syndrome. This is an X-linked condition characterized by overgrowth, and various visceral and skeletal dysmorphisms. The phenotype of the Simpson-Golabi-Behmel syndrome patients and GPC3-deficient mice, as well as gene transfection experiments indicate that GPC3 can act as an inhibitor of cell proliferation and survival. It has been previously shown that GPC3 expression is downregulated in mesotheliomas and ovarian cancer. Here we report that GPC3 expression is also silenced in human breast cancer, and that this silencing is due, at least in part, to hypermethylation of the GPC3 promoter. Ectopic expression of GPC3 inhibited growth in eight out of 10 breast cancer cell lines. Collectively, these data suggest that GPC3 can act as a negative regulator of breast cancer growth.

L23 ANSWER 9 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2001407894 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11454708
TITLE: Glypican-1 is overexpressed in human breast cancer and modulates the mitogenic effects of multiple heparin-binding growth factors in breast cancer cells.
AUTHOR: Matsuda K; Maruyama H; Guo F; Kleeff J; Itakura J; Matsumoto Y; Lander A D; Korc M
CORPORATE SOURCE: Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Biological Chemistry, and Pharmacology, University of California, Irvine, California 92697, USA.
CONTRACT NUMBER: CA-40162 (NCI)
NS-26862 (NINDS)
SOURCE: Cancer research, (2001 Jul 15) Vol. 61, No. 14, pp. 5562-9.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802
ED Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802
AB Glypicans are a family of glycosylphosphatidylinositol-anchored cell

surface heparan sulfate proteoglycans implicated in the control of cellular growth and differentiation. Here we show that glypican-1 is strongly expressed in human breast cancers, whereas expression of glypican-1 is low in normal breast tissues. In contrast, the expression of glypican-3 and -4 is only slightly increased in breast cancers by comparison with normal breast tissues, and glypican-2 and -5 are below the level of detection by Northern blotting in both normal and cancer samples. Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with phosphoinositide-specific phospholipase-C abrogated the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor and fibroblast growth factor 2. Stable transfection of these cells with a glypican-1 antisense construct markedly decreased glypican-1 protein levels and the mitogenic response to the same heparin-binding growth factors, as well as that to heregulin alpha, heregulin beta, and hepatocyte growth factor. Syndecan-1 was also expressed at high levels in both breast cancer tissues and breast cancer cells when compared with normal breast tissues. There was a good correlation between glypican-1 and syndecan-1 expression in the tumors. However, clones expressing the glypican-1 antisense construct did not exhibit decreased syndecan-1 levels, indicating that loss of responsiveness to heparin-binding growth factors in these clones was not due to altered syndecan-1 expression. Furthermore, 8 of 10 tumors with stage 2 or 3 disease exhibited high levels of glypican-1 by Northern blot analysis. In contrast, low levels of glypican-1 mRNA were evident in 1 of 10 tumors with stage 2 or 3 disease and in 9 of 10 tumors with stage 1 disease. Taken together, these data suggest that glypican-1 may play a pivotal role in the ability of breast cancer cells to exhibit a mitogenic response to multiple heparin-binding growth factors and may contribute to disease progression in this malignancy.

L23 ANSWER 10 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1999433578 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10505759
TITLE: Stable transfection of a glypican-1 antisense construct decreases tumorigenicity in PANC-1 pancreatic carcinoma cells.
AUTHOR: Kleeff J; Wildi S; Kumbasar A; Friess H; Lander A D; Korc M
CORPORATE SOURCE: Department of Medicine, University of California, Irvine 92697, USA.
CONTRACT NUMBER: CA-40162 (NCI)
SOURCE: Pancreas, (1999 Oct) Vol. 19, No. 3, pp. 281-8. Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991123
ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991123
AB Glypican-1 belongs to a family of glycosylphosphatidylinositol (GPI)-anchored heparan sulfate proteoglycans (HSPGs) that affect cell growth, invasion, and adhesion. Cell-surface HSPGs are believed to act as co-receptors for heparin-binding mitogenic growth factors. It

was reported that glypican-1 is strongly expressed in human pancreatic cancer, and that it may play an essential role in regulating growth-factor responsiveness in pancreatic carcinoma cells. In this study we investigated the effects of decreased glypican-1 expression in PANC-1 pancreatic cancer cells. To this end, PANC-1 cells were stable transfected with a full-length glypican-1 antisense construct. The glypican- antisense transfected clones displayed markedly reduced glypican- protein levels and a marked attenuation of the mitogenic responses to heparin-binding growth factors that are commonly overexpressed in pancreatic cancer: fibroblast growth factor-2 (FGF2), heparin-binding epidermal growth factor (EGF)-like growth factor (HB-EGF), and hepatocyte growth factor (HGF). In addition, glypican-1 antisense-expressing PANC-1 cells exhibited a significantly reduced ability to form tumors in nude mice in comparison with parental and sham-transfected PANC-1 cells. These data suggest that glypican-1 plays an important role in the responses of pancreatic cancer cells to heparin-binding growth factors, and documents for the first time that its expression may enhance tumorigenic potential in vivo.

L23 ANSWER 11 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1999127849 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9930659
TITLE: Role of heparan sulphate proteoglycans in the regulation of human lactoferrin binding and activity in the MDA-MB-231 breast cancer cell line.
AUTHOR: Damiens E; El Yazidi I; Mazurier J; Elass-Rochard E; Duthille I; Spik G; Boilly-Marer Y
CORPORATE SOURCE: Laboratoire de Chimie Biologique, UMR du CNRS 111, Universite des Sciences et Technologies de Lille, Villeneuve d'Ascq, France.
SOURCE: European journal of cell biology, (1998 Dec) Vol. 77, No. 4, pp. 344-51.
Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413
ED Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413
AB We previously demonstrated that lactoferrin increases breast cell sensitivity to natural killer cell cytotoxicity whereas haematopoietic cells are unaffected by lactoferrin. It has been described that lactoferrin binds to various glycosaminoglycans. Compared to haematopoietic cells, breast cancer cells and particularly the breast cell line MDA-MB-231, possess a high level of proteoglycans. Scatchard analysis of 125I-lactoferrin binding to MDA-MB-231 cells revealed the presence of two classes of binding sites: a low affinity site with a Kd of about 700 nM and 3.9 x 10(6) sites and a higher affinity class with a Kd of 45 nM and 2.9 x 10(5) sites per cell. To investigate the potential regulation of lactoferrin activity by proteoglycans expressed on the MDA-MB-231 cells, we treated these cells with glycosaminoglycan-degrading enzymes or sodium chlorate, a metabolic inhibitor of proteoglycan sulphation. We showed that chondroitinase treatment has no effect, while heparinase or chlorate

treatment significantly reduces both the binding of lactoferrin to cell surface sulphated molecules such as heparan sulphate proteoglycans (HSPG) and the affinity of lactoferrin for the higher affinity binding sites. The modulation of the lactoferrin binding was correlated with a decrease in lactoferrin activities on both MDA-MB-231 cell sensitisation to lysis and proliferation. Taken together, these results suggest that the presence of adequately sulphated molecules, in particular HSPG, is important for lactoferrin interaction and activity on the breast cancer cells MDA-MB-231.

L23 ANSWER 12 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1999076030 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9858933
TITLE: Morphological aspects of altered basement membrane metabolism in invasive carcinomas of the breast and the larynx.
AUTHOR: Nerlich A G; Lebeau A; Hagedorn H G; Sauer U; Schleicher E D
CORPORATE SOURCE: Pathologisches Institut, Universitat Munchen, Germany.. Andreas.Nerlich@lrz.uni-muenchen.de
SOURCE: Anticancer research, (1998 Sep-Oct) Vol. 18, No. 5A, pp. 3515-20.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981229

ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981229

AB In the present study we compared the localization of major basement membrane (BM) components and their mRNAs between invasive carcinomas of the breast (adenocarcinomas) and larynx carcinomas (squamous cell carcinomas, SCC), in order to determine the extent of BM production and deposition in malignant tumors of biologically different behaviour. Thus, breast carcinomas usually show a rapid locoregional/systemic spread, while the laryngeal SCCs normally show a more locally restricted growth pattern. While normal mammary glands and laryngeal mucosa revealed an intact epithelial BM as evidenced by a continuous linear staining for collagen IV, laminin-1, heparan sulfate proteoglycan (perlecan) and fibronectin-as well as collagen VII in the larynx mucosa-, this continuous staining was lost in the invasive carcinomas, however, affecting the two tumor types differently. In the breast carcinomas, a complete loss was seen even in well differentiated tumors affecting the various BM components similarly, while in the SCCs well differentiated carcinomas had retained significantly more BM material than poorly differentiated ones. In the SCCs, an "early" loss of collagen VII contrasted with a "later" loss of collagen IV, laminin, perlecan and fibronectin the extent of which was, however, associated with a decreasing degree of differentiation. In contrast to the protein findings, by use of the in-situ hybridization we observed a significant expression of mRNA for collagen IV, perlecan and fibronectin. The resulting pattern was comparable between both tumor types and not significantly related to the tumor cell differentiation. Both tumor cells and stroma cells

were positively labelled with a more extensive labelling of the stroma cells. Our observations indicate a similar upregulation of the mRNAs for BM-components in breast and larynx carcinomas, but significant differences in the BM-protein deposition so that either major differences in presumed BM-proteolysis or further translational defects are suggested. Furthermore, it can be speculated that the far lesser amount of BM-material in the breast carcinomas may be linked to the more aggressive metastatic spread of those tumors, particularly when compared to the SCCs.

L23 ANSWER 13 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1999069148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9851863
TITLE: Alterations in both heparan sulfate proteoglycans and mitogenic activity of fibroblast growth factor-2 are triggered by inhibitors of proliferation in normal and breast cancer epithelial cells.
AUTHOR: Lambrecht V; Le Bourhis X; Toillon R A; Boilly B; Hondermarck H
CORPORATE SOURCE: Unite de Dynamique des Cellules Embryonnaires et Cancereuses, Batiment SN3, Universite des Sciences et Technologies de Lille, Villeneuve d'Ascq Cedex, 59655, France.
SOURCE: Experimental cell research, (1998 Dec 15) Vol. 245, No. 2, pp. 239-44.
Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990202
Last Updated on STN: 20000303
Entered Medline: 19990119
ED Entered STN: 19990202
Last Updated on STN: 20000303
Entered Medline: 19990119
AB Heparan sulfate proteoglycans (HSPG) are involved in the regulation of cellular proliferation, differentiation, and migration. We have studied the effect of three inhibitors of proliferation on 35S incorporation into HSPG of the breast cancer cell lines MCF-7 and MDA-MB-231 and the normal breast epithelial cells (NBEC). Transforming growth factor beta-1 (TGFbeta-1), which inhibits the proliferation of NBEC, but not of MCF-7 and MDA-MB-231, cells induced an increase in 35S incorporation of HSPG in NBEC, but had no effect on cancer cells. Sodium butyrate (NaB), which inhibits NBEC as well as cancer cell proliferation, induced an increase in 35S incorporation into HSPG in all cell types studied. In contrast, retinoic acid had no effect on HSPG of breast epithelial cells. Modification of HSPG induced by TGFbeta-1 or NaB treatments in normal and breast cancer epithelial cells resulted in an increase in 125I-fibroblast growth factor-2 (FGF-2) binding on HSPG. More importantly, NaB pretreatment resulted in an inhibition of the MCF-7 cell responsiveness to FGF-2, even though these cells remained sensitive to growth stimulation induced by serum or epidermal growth factor. These results indicate that changes in HSPG production are a key process involved in the mechanism of breast epithelial cell growth regulation.
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L23 ANSWER 14 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1999021665 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9802880
TITLE: The cell-surface heparan sulfate proteoglycan glypican-1 regulates growth factor action in pancreatic carcinoma cells and is overexpressed in human pancreatic cancer.
AUTHOR: Kleeff J; Ishiwata T; Kumbasar A; Friess H; Buchler M W; Lander A D; Korc M
CORPORATE SOURCE: Departments of Medicine, Biological Chemistry, and Pharmacology, University of California, 92697, USA.
CONTRACT NUMBER: CA-40162 (NCI)
NS-26862 (NINDS)
SOURCE: The Journal of clinical investigation, (1998 Nov 1) Vol. 102, No. 9, pp. 1662-73.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981221
ED Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981221
AB Heparan sulfate proteoglycans (HSPGs) play diverse roles in cell recognition, growth, and adhesion. In vitro studies suggest that cell-surface HSPGs act as coreceptors for heparin-binding mitogenic growth factors. Here we show that the glycosylphosphatidylinositol- (GPI-) anchored HSPG glypican-1 is strongly expressed in human pancreatic cancer, both by the cancer cells and the adjacent fibroblasts, whereas expression of glypican-1 is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic cancer cell lines, which express glypican-1, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors that are commonly overexpressed in pancreatic cancer: fibroblast growth factor 2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). PI-PLC did not alter the response to the non-heparin-binding growth factors EGF and IGF-1. Stable expression of a form of glypican-1 engineered to possess a transmembrane domain instead of a GPI anchor conferred resistance to the inhibitory effects of PI-PLC on growth factor responsiveness. Furthermore, transfection of a glypican-1 antisense construct attenuated glypican-1 protein levels and the mitogenic response to FGF2 and HB-EGF. We propose that glypican-1 plays an essential role in the responses of pancreatic cancer cells to certain mitogenic stimuli, that it is relatively unique in relation to other HSPGs, and that its expression by pancreatic cancer cells may be of importance in the pathobiology of this disorder.

L23 ANSWER 15 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1998226639 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9558337
TITLE: Hepatocyte growth factor/scatter factor has distinct classes of binding site in heparan sulfate from mammary cells.
AUTHOR: Rahmoune H; Rudland P S; Gallagher J T; Fernig D G

CORPORATE SOURCE: School of Biological Sciences, Life Sciences Building, University of Liverpool, U.K.
SOURCE: Biochemistry, (1998 Apr 28) Vol. 37, No. 17, pp. 6003-8.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19990129
Entered Medline: 19980520

ED Entered STN: 19980529
Last Updated on STN: 19990129
Entered Medline: 19980520

AB Hepatocyte growth factor/scatter factor (HGF/SF) is a heparan sulfate (HS)-binding growth factor and morphogen for mammary epithelial cells that is produced by mammary stromal fibroblasts. HS chains, purified as peptidoglycans from a panel of cell lines representative of the ductal epithelial cell (Huma 123), the myoepithelial cell (Huma 109), the stromal fibroblast (Rama 27), and malignant mammary epithelial cells (MCF-7 and ZR-75), were used in a biosensor-based assay to identify the classes of HGF/SF-binding sites in the polysaccharide chains. At least three distinct binding sites were identified. One site exhibits fast association and fast dissociation kinetics [kass (1.4-7.7) x 10(6) M-1 s-1; kdiss 0. 0032-0.0096 s-1] and is present on the HS from benign Huma 123 epithelial cells, Huma 109 myoepithelial-like cells, and ZR-75 malignant cells. The second binding site, found on HS from the malignant MCF-7 cells, has slower HGF/SF-binding kinetics (kass 0.20 x 10(6) M-1 s-1; kdiss 0.00055 s-1). The third binding site possesses fast association and slow dissociation kinetics (kass 1.1 x 10(6) M-1 s-1; kdiss 0.00020 s-1) and was found on the HS isolated from the culture medium of the Huma 123 benign epithelial cells. The first and second binding sites have a similar Kd, 1-3 nM, while the third binding site has a considerably higher affinity for HGF/SF (Kd 200 pM). The three binding sites seem to be mutually exclusive, since each sample of HS possessed just one of the sites.

L23 ANSWER 16 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1998217538 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9556792
TITLE: [Value of basement membrane imaging in diagnosis of invasive carcinomas].
Wert der Basalmembrandarstellung in der Diagnostik invasiver Karzinome.
AUTHOR: Nerlich A G
CORPORATE SOURCE: Pathologisches Institut, Universitat Munchen.
SOURCE: Der Pathologe, (1998 Feb) Vol. 19, No. 2, pp. 89-94.
Ref: 28
Journal code: 8006541. ISSN: 0172-8113.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708

Searcher : Shears 571-272-2528

Last Updated on STN: 19980708
Entered Medline: 19980623

ED Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980623

AB The destruction of the epithelial basement membrane is widely regarded as a clear criterion for invasive malignant tumor growth. Since, however, defects in the basement membrane may also occur in non-invasive conditions, such as inflammatory and proliferative lesions, and since it has been shown that particularly in highly differentiated squamous cell carcinomas a continuous basement membrane is mimicked by the presence of isolated components, this criterion seems to be of minor value for the diagnosis of malignancy. Despite these drawbacks, the immunolocalization of basement membrane material may still be of differential diagnostic significance in certain situations. This holds particularly true for invasive (ductal) breast carcinomas, which usually completely lack a basement membrane. Accordingly, sclerosing adenosis can be distinguished from invasive carcinoma, as a distinction can be made between neoplastic (malignant) tubular formations and reactive lesions.

L23 ANSWER 17 OF 22 MEDLINE on STN
ACCESSION NUMBER: 1998155651 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9494547
TITLE: Gene expression and protein deposition of major basement membrane components and TGF-beta 1 in human breast cancer.
AUTHOR: Nerlich A G; Wiest I; Wagner E; Sauer U; Schleicher E D
CORPORATE SOURCE: Pathologisches Institut, Universitat Munchen, Germany.. u7912ag@sunmail.lrz-muenchen.de
SOURCE: Anticancer research, (1997 Nov-Dec) Vol. 17, No. 6D, pp. 4443-9.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980326

ED Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980326

AB In the present study we used immunohistochemistry and in-situ hybridization for the localization of major basement membrane (BM) components and their mRNA, respectively, in order to determine the extent of BM production and deposition in normal mammary tissue as well as in invasive mamma carcinomas. While normal mammary tissue showed an intact epithelial BM, as evidenced by a continuous linear staining for collagen i.v., laminin, heparan sulfate proteoglycan (perlecan) and fibronectin, this staining was widely lost in the invasive carcinomas. Non-invasive intraductal areas of the carcinomas (carcinoma-in-situ) revealed focal fragmentation and duplication of the epithelial BM. Using in-situ hybridization, we observed only focally positive mRNA-expression for collagen i.v.-, perlecan- and fibronectin-mRNA in normal glands, while mRNA-signals were significantly enhanced in one case of fibroadenoma and particularly in invasive and non-invasive carcinomas, regardless of the degree of

tumor cell differentiation. In these instances both tumor and stroma cells were positively labelled. In addition, we could demonstrate a significant increase in the level of TGF-beta 1-mRNA--as the most active cytokine for the induction of matrix component production--by carcinoma cells and to lesser extent by stroma cells. The discrepancy between significantly enhanced mRNA-synthesis and loss in protein deposition points either to an upregulated activity of matrix degrading proteinases (matrix-metalloproteinases) or a posttranslational block of protein synthesis or both.

L23 ANSWER 18 OF 22 MEDLINE on STN
ACCESSION NUMBER: 97141426 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8986623
TITLE: Heparan sulfate proteoglycans play a dual role in regulating fibroblast growth factor-2 mitogenic activity in human breast cancer cells.
AUTHOR: Delehedde M; Deudon E; Boilly B; Hondermarck H
CORPORATE SOURCE: Unite de Dynamique des Cellules Embryonnaires et Cancereuses, Universite des Sciences et Technologies de Lille, Villeneuve d'Ascq Cedex, 59655, France.. Hubert.Hondermarck@univ-lille1.fr
SOURCE: Experimental cell research, (1996 Dec 15) Vol. 229, No. 2, pp. 398-406.
Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19980206
Entered Medline: 19970206

ED Entered STN: 19970219
Last Updated on STN: 19980206
Entered Medline: 19970206

AB The human breast cancer cell lines MCF-7 and MDA-MB-231 differ in their responsiveness to fibroblast growth factor-2 (FGF-2). This growth factor stimulates proliferation in well-differentiated MCF-7 cells, whereas the less well-differentiated MDA-MB-231 cells are insensitive to this molecule. To investigate the potential regulation of FGF-2 mitogenic activity by heparan sulfate proteoglycans (HSPG), we have treated human breast cancer cells by glycosaminoglycan degrading enzymes or a metabolic inhibitor of proteoglycan sulfation: sodium chlorate. The interaction between FGF-2 and proteoglycans was assayed by examining the binding of 125I-FGF-2 to breast cancer cell cultures as well as to cationic membranes loaded with HSPG. Using MCF-7 cells, we showed that heparinase treatment inhibited FGF-2 binding to HSPG and completely abolished FGF-2 induced growth; chlorate treatment of MCF-7 cells decreased FGF-2 binding to HSPG and cell responsiveness in a dose-dependent manner. This demonstrates a requirement of adequately sulfated HSPG for FGF-2 growth-promoting activity on MCF-7 cells. In highly invasive MDA-MB-231 cells which produce twice as much HSPG as MCF-7 cells and which are not normally responsive to exogenously added FGF-2, chlorate treatment decreased FGF-2 binding to HSPG and induced FGF-2 mitogenic effect. This chlorate effect was dose dependent and observed at concentrations of 10-30 mM; higher chlorate concentrations completely abolished the FGF-2 effect. This shows that the HSPG level of sulfation can also negatively regulate the biological activity of FGF-2. Taken together,

these results demonstrate a crucial role for HSPG in both positive and negative control of FGF-2 mitogenic activity in breast cancer cell proliferation.

L23 ANSWER 19 OF 22 MEDLINE on STN
ACCESSION NUMBER: 96256115 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8652906
TITLE: [Involvement of sulfated proteoglycans in the control of proliferation of MCF-7 breast cancer cells]. Implication des proteoglycanes sulfates dans le controle de la proliferation des cellules cancereuses mammaires MCF-7.
AUTHOR: Delehedde M; Deudon E; Boilly B; Hondermarck H
CORPORATE SOURCE: Laboratoire de biologie cellulaire et moleculaire du developpement, Universite des sciences et technologies de Lille, France.
SOURCE: Bulletin du cancer, (1996 Feb) Vol. 83, No. 2, pp. 129-34.
Journal code: 0072416. ISSN: 0007-4551.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960808
Last Updated on STN: 19980206
Entered Medline: 19960731
ED Entered STN: 19960808
Last Updated on STN: 19980206
Entered Medline: 19960731
AB The MCF-7 breast cancer cells exhibit remarkable growth enhancement in response to basic fibroblast growth factor (FGF-2) stimulation in a dose dependent manner. To investigate the involvement of proteoglycans on control of FGF-2 induced proliferation, polysaccharide chains were degraded by specific enzymes. Our results showed that MCF-7 cells were unsensitive to FGF-2 after enzymatic degradation of heparin sulfate proteoglycans (HSPG) by heparinase. After metabolic inhibition of sulphation by sodium chloride, radiolabelled proteoglycans were purified and quantified by ion exchange chromatography. Sodium chlorate treatment reduced by 70% sulfation of proteoglycans. This decrease of sulphation totally inhibited FGF-2-mediated proliferation. The sulphated glycosaminoglycans which were critical in FGF-2-induced proliferation were strictly HSPG, as an addition of heparin in cell culture medium can restore FGF-2 mitogenic activity. In contrast, other glycosaminoglycans (chondroitin sulfate/hyaluronic acid) did not show any effect. These results provide clear evidence for the critical role of HSPG in FGF-2-induced proliferation on MCF-7 breast cancer cells.

L23 ANSWER 20 OF 22 MEDLINE on STN
ACCESSION NUMBER: 95148582 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7846019
TITLE: Immunohistochemical study of heparan sulfate proteoglycan in adenocarcinomas of the pancreas.
AUTHOR: Wang Z H; Manabe T; Ohshio G; Imamura T; Yoshimura T; Suwa H; Ishigami S; Kyogoku T
CORPORATE SOURCE: First Department of Surgery, Faculty of Medicine, Kyoto University, Japan.

Searcher : Shears 571-272-2528

SOURCE: Pancreas, (1994 Nov) Vol. 9, No. 6, pp. 758-63.
Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950316
Last Updated on STN: 19980206
Entered Medline: 19950308

ED Entered STN: 19950316
Last Updated on STN: 19980206
Entered Medline: 19950308

AB The prognosis for carcinoma of the pancreas is extremely poor. One of the characteristics of this tumor is its invasion of the surrounding tissues. Reduction of glycoprotein is considered to be conducive to invasion of the basement membrane by carcinoma cells. Heparan sulfate proteoglycan (HSPG), a kind of glycoprotein, is an important component of basement membrane. In this study, the relation between HSPG and carcinoma of the pancreas was examined by using the immunohistochemical method, and the survival rate of pancreatic adenocarcinoma was evaluated. We found that some carcinomas contained little or no HSPG. The poorer the differentiation of an adenocarcinoma of the pancreas, the lower was its content of HSPG. The level of HSPG was significantly different in carcinomatous and in noncarcinomatous cells. There was a close correlation among the content of HSPG, the degree of differentiation of carcinomas of the pancreas, and the survival time. HSPG seems to be useful in prognosis of adenocarcinoma of the pancreas.

L23 ANSWER 21 OF 22 MEDLINE on STN
ACCESSION NUMBER: 94245776 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8188731
TITLE: Calcium regulation of heparan sulfate proteoglycans in breast cancer cells.
AUTHOR: Vandewalle B; Revillion F; Hornez L; Lefebvre J
CORPORATE SOURCE: Laboratoire d'Endocrinologie Experimentale, Centre Oscar Lambret, Lille, France.
SOURCE: Journal of cancer research and clinical oncology, (1994) Vol. 120, No. 7, pp. 389-92.
Journal code: 7902060. ISSN: 0171-5216.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940629
Last Updated on STN: 19980206
Entered Medline: 19940620

ED Entered STN: 19940629
Last Updated on STN: 19980206
Entered Medline: 19940620

AB Breast tumor cells have been shown to be responsive to calcium in that external calcium modifies cell calcium, shape and growth. In order to highlight some of the numerous mechanisms by which calcium is operating, we investigated its influence on the cell microenvironment and particularly its effect on membrane-associated heparan sulfate proteoglycans. The breast cancer cells MCF-7 were grown either at low (0.04 mM) or high (2.5 mM) calcium concentration. After 3 days of

culture, cells were labeled with Na2(35)SO4 for 24 h and cell-associated proteoglycans extracted and purified. We showed that calcium enhances approximately twofold the synthesis of sulfated proteoglycans and, among these sulfated proteoglycans, chemical treatments indicated a specific two- to threefold increase of heparan sulfate proteoglycans. In view of the increasing implication of heparan sulfate proteoglycans in numerous mechanisms such as cell-cell contact, cell-matrix interactions and cell growth control, it appears that calcium may be a target for modulating metastatic and growth processes in breast tumor cells.

L23 ANSWER 22 OF 22 MEDLINE on STN
ACCESSION NUMBER: 94058117 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8239544
TITLE: Influence of cAMP on E-cadherin expression and cell surface heparan sulfate proteoglycan synthesis in human breast cancer cells.
AUTHOR: Revillion F; Vandewalle B; Hornez L; Lefebvre J
CORPORATE SOURCE: Laboratoire d'Endocrinologie Experimentale, Centre Oscar Lambret, Lille, France.
SOURCE: Anticancer research, (1993 Sep-Oct) Vol. 13, No. 5A, pp. 1625-9.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19980206
Entered Medline: 19931217
ED Entered STN: 19940117
Last Updated on STN: 19980206
Entered Medline: 19931217
AB The growth of MCF-7 and MDA-MB-231 human breast cancer cells was inhibited by treatment with dibutyryl cAMP (dBcAMP, 10(-4) M). The effects on E-cadherin expression and cell surface associated heparan sulfate proteoglycans (HSPG) synthesis, both implicated in cell adhesion, were investigated. dBcAMP was demonstrated to increase E-cadherin expression in the E-cadherin positive MCF-7 cells. However, in the E-cadherin negative MDA-MB-231 cells, the treatment did not induce expression of this cell adhesion molecule. Furthermore, in the two cell lines, an increase of the [35S] Na2SO4 incorporation into the cell surface sulfated PG was observed subsequently to dBcAMP treatment. Interestingly, the proportion of cell surface HSPG was also enhanced by this treatment. Taken together, these results demonstrate that the decrease of the proliferation observed in the human breast cancer cells after dBcAMP treatment is associated with an increase in the cell-cell and cell-matrix interactions. This suggests that the metastatic process which involves lack of cohesiveness and migration of the cells may probably be counteracted by cAMP in the human breast cancer cells.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 17:45:46 ON 16 MAR 2006)
L25 1453 SEA ABB=ON PLU=ON "KORC M"?/AU -Author
L26 540 SEA ABB=ON PLU=ON "LANDER A"?/AU
L27 34 SEA ABB=ON PLU=ON L25 AND L26
L28 1959 SEA ABB=ON PLU=ON L25 OR L26

Searcher : Shears 571-272-2528

L29 167 SEA ABB=ON PLU=ON L28 AND (L2 OR L8)
L30 43 SEA ABB=ON PLU=ON L29 AND (CANCER? OR CARCIN? OR TUMOUR OR TUMOR OR NEOPLAS?)(S)(PANCREAS OR PANCREAT? OR BREAST OR MAMMAR?)
L31 54 SEA ABB=ON PLU=ON L27 OR L30
L32 15 DUP REM L31 (39 DUPLICATES REMOVED)

L32 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:1263638 CAPLUS
DOCUMENT NUMBER: 144:85561
TITLE: Growth factor-induced shedding of syndecan-1 confers **glypican-1** dependence on mitogenic responses of cancer cells
AUTHOR(S): Ding, Kan; Lopez-Burks, Martha; Sanchez-Duran, Jose Antonio; **Korc, Murray; Lander, Arthur D.**
CORPORATE SOURCE: Department of Developmental and Cell Biology, University of California, Irvine, Irvine, CA, 92697, USA
SOURCE: Journal of Cell Biology (2005), 171(4), 729-738
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The cell surface **heparan sulfate proteoglycan (HSPG) glypican-1** is up-regulated by **pancreatic** and **breast cancer** cells, and its removal renders such cells insensitive to many growth factors. We sought to explain why the cell surface **HSPG** syndecan-1, which is also up-regulated by these cells and is a known growth factor coreceptor, does not compensate for **glypican-1** loss. We show that the initial responses of these cells to the growth factor FGF2 are not glypican dependent, but they become so over time as FGF2 induces shedding of syndecan-1. Manipulations that retain syndecan-1 on the cell surface make long-term FGF2 responses glypican independent, whereas those that trigger syndecan-1 shedding make initial FGF2 responses glypican dependent. We further show that syndecan-1 shedding mediated by matrix metalloproteinase-7 (MMP7), which, being anchored to cells by **HSPGs**, also causes its own release in a complex with syndecan-1 ectodomains. These results support a specific role for shed syndecan-1 or MMP7-syndecan-1 complexes in tumor progression and add to accumulating evidence that syndecans and glypicans have nonequivalent functions in vivo.
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:627623 CAPLUS
DOCUMENT NUMBER: 141:259008
TITLE: Membrane-Associated **Heparan Sulfate Proteoglycans** Are Involved in the Recognition of Cellular Targets by NKp30 and NKp46
AUTHOR(S): Bloushtain, Noga; Qimron, Udi; Bar-Ilan, Ahuva; Hershkovitz, Oren; Gazit, Roi; Fima, Eyal; **Korc, Murray**; Vlodavsky, Israel; Bovin, Nicolai V.; Porgador, Angel

CORPORATE SOURCE: Department of Microbiology and Immunology, Faculty of Health Sciences, and the Cancer Research Center, Ben Gurion University of the Negev, Beer Sheva, Israel
SOURCE: Journal of Immunology (2004), 173(4), 2392-2401
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lysis of virus-infected and tumor cells by NK cells is mediated via natural cytotoxicity receptors (NCRs). The authors have recently shown that the NKp44 and NKp46 NCRs, but not the NKp30, recognize viral hemagglutinins. In this study the authors explored the nature of the cellular ligands recognized by the NKp30 and NKp46 NCRs. The authors demonstrate that target cell surface **heparan sulfate proteoglycans** (**HSPGs**) are recognized by NKp30 and NKp46 and that 6-O-sulfation and N-acetylation state of the glucose building unit affect this recognition and lysis by NK cells. **Tumor** cells expressing cell surface heparanase, CHO cells lacking membranal heparan sulfate and **glypican-1**-suppressed **pancreatic cancer** cells manifest reduced recognition by NKp30 and NKp46 and are lysed to a lesser extent by NK cells. The results are the first clue for the identity of the ligands for NKp30 and NKp46. Whether the ligands are particular **HSPGs**, unusual heparan sulfate epitopes, or a complex of **HSPGs** and either other protein or lipid moieties remains to be further explored.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:563110 CAPLUS
DOCUMENT NUMBER: 141:134658
TITLE: **Glypican-1** antisense transfection modulates TGF-β-dependent signaling in Colo-357 **pancreatic cancer** cells
AUTHOR(S): Li, Junsheng; Kleeff, Joerg; Kayed, Hany; Felix, Klaus; Penzel, Roland; Buechler, Markus W.; **Korc, Murray**; Friess, Helmut
CORPORATE SOURCE: Department of General Surgery, University of Heidelberg, Heidelberg, Germany
SOURCE: Biochemical and Biophysical Research Communications (2004), 320(4), 1148-1155
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **heparan sulfate proteoglycan** **glypican-1** is essential as a co-receptor for heparin binding growth factors, such as HB-EGF and FGF-2, in **pancreatic cancer** cells. In the present study, the role of **glypican-1** in the regulation of TGF-β signaling was investigated. Colo-357 **pancreatic cancer** cells were stably transfected with a full-length **glypican-1** antisense construct. Cell growth was determined by MTT and soft agar assays. TGF-β1 induced p21 expression and Smad2 phosphorylation were analyzed by immunoblotting. PAI-1

promoter activity was determined by luciferase assays. Down-regulation of **glypican-1** expression by stable transfection of a full-length **glypican-1** antisense construct resulted in decreased anchorage-dependent and -independent cell growth in Colo-357 **pancreatic cancer** cells and attenuated TGF-β1 induced cell growth inhibition, Smad2 phosphorylation, and PAI-1 promoter activity. There was, however, no significant difference in TGF-β1 induced p21 expression and Smad2 nuclear translocation. In conclusion, **glypican-1** is required for efficient TGF-β1 signaling in **pancreatic cancer** cells.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2003:435071 CAPLUS
DOCUMENT NUMBER: 139:3235
TITLE: **Glypican-1** determination and modulation in human **breast cancer** diagnosis and treatment
INVENTOR(S): **Korc, Murray; Lander, Arthur D.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U. S. Ser. No. 807,575.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003103980	A1	20030605	US 2002-210327	20020731
WO 2000023109	A1	20000427	WO 1999-US24176	19991015

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1998-104510P	P	19981016
US 1999-121624P	P	19990225
WO 1999-US24176	W	19991015
US 2001-807575	A2	20010712
US 2001-309722P	P	20010731

AB Glycosylphosphatidylinositol- (GPI-) anchored **heparan sulfate proteoglycan** (**HSPG**) **glypican-1** is strongly expressed in human **breast** and **pancreatic cancer**-both by the **cancer** cells and, in the case of **pancreatic**

cancer, the adjacent fibroblasts-whereas expression of **glypican-1** is low in the normal **pancreas** and in chronic **pancreatitis**. Treatment of two **pancreatic cancer** cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 **breast cancer** cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in **breast cancer** tissues as well as **breast cancer** cells by comparison with **breast** normal tissues. Temporary or permanent transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein levels and the mitogenic response to FGF2 and HB-EGF. Glypican can be used to detect the carcinoma in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense constructs) of surface of the extracellular domain of **glypican-1** are effective in retarding the growth of glypican-responsive carcinomas. By immunohistochem., strong **glypican-1** immunoreactivity was present in a heterogeneous pattern in the cancer cells forming intraductal and lobular carcinomas, and in the fibroblasts surrounding the cancer cells but not in the fibroblasts that were more distant from the tumor. A moderate to strong **glypican-1** mRNA in situ hybridization signal was also present in the cancer cells, and, to a lesser extent, in the fibroblasts immediately adjacent to the cancer cells. These observations suggest that **breast cancer** cells produce and release **glypican-1**, and that some of the **glypican-1** present in the fibroblasts surrounding the **breast cancer** cells in vivo derives from the **cancer** cells.

L32 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:419974 BIOSIS
DOCUMENT NUMBER: PREV200200419974
TITLE: Growth factors and signaling events in **pancreatic cancer**.
AUTHOR(S): **Korc, Murray** [Reprint author]
CORPORATE SOURCE: University of California, Irvine, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 1170. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002

L32 ANSWER 6 OF 15 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation

on STN
ACCESSION NUMBER: 2002:415543 SCISEARCH
THE GENUINE ARTICLE: 548AW
TITLE: Overexpression of FGF type I receptor enhances surface retention of glypican-1 and FGF-2 dependent signaling.
AUTHOR: Matsuda K (Reprint); Lopez M; Fukahi K; **Lander A; Korc M**
SOURCE: GASTROENTEROLOGY, (APR 2002) Vol. 122, No. 4, Supp. [1], pp. A139-A139. MA S981.
ISSN: 0016-5085.
PUBLISHER: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 31 May 2002
Last Updated on STN: 31 May 2002

L32 ANSWER 7 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:518654 BIOSIS
DOCUMENT NUMBER: PREV200200518654
TITLE: Overexpression of FGF type I receptor enhances surface retention of glypican-1 and FGF-2 dependent signaling.
AUTHOR(S): Matsuda, Kei [Reprint author]; Lopez, Martha [Reprint author]; Fukahi, Kimi [Reprint author]; **Lander, Arthur** [Reprint author]; **Korc, Murray** [Reprint author]
CORPORATE SOURCE: Irvine, CA, USA
SOURCE: Gastroenterology, (April, 2002) Vol. 122, No. 4 Suppl. 1, pp. A-139. print.
Meeting Info.: Digestive Disease Week and the 103rd Annual Meeting of the American Gastroenterological Association. San Francisco, CA, USA. May 19-22, 2002.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

L32 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2001:544238 CAPLUS
DOCUMENT NUMBER: 135:240061
TITLE: **Glypican-1** is overexpressed in human **breast cancer** and modulates the mitogenic effects of multiple heparin-binding growth factors in **breast cancer** cells
AUTHOR(S): Matsuda, Kei; Maruyama, Haruhisa; Guo, Fang; Kleeff, Jorg; Itakura, Jun; Matsumoto, Yoshiro; **Lander, Arthur D.; Korc, Murray**
CORPORATE SOURCE: Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Biological Chemistry, University of California, Irvine, CA, 92697, USA
SOURCE: Cancer Research (2001), 61(14), 5562-5569
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glypicans are a family of glycosylphosphatidylinositol-anchored cell surface **heparan sulfate proteoglycans** implicated in the control of cellular growth and differentiation. Here we show that **glypican-1** is strongly expressed in human **breast cancers**, whereas expression of **glypican-1** is low in normal **breast** tissues. In contrast, the expression of glypican-3 and -4 is only slightly increased in **breast cancers** by comparison with normal **breast** tissues, and glypican-2 and -5 are below the level of detection by Northern blotting in both normal and **cancer** samples. Treatment of MDA-MB-231 and MDA-MB-468 **breast cancer** cells with phosphoinositide-specific phospholipase-C abrogated the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor and fibroblast growth factor 2. Stable transfection of these cells with a **glypican-1** antisense construct markedly decreased **glypican-1** protein levels and the mitogenic response to the same heparin-binding growth factors, as well as that to heregulin α, heregulin β, and hepatocyte growth factor. Syndecan-1 was also expressed at high levels in both **breast cancer** tissues and **breast cancer** cells when compared with normal **breast** tissues. There was a good correlation between **glypican-1** and syndecan-1 expression in the tumors. However, clones expressing the **glypican-1** antisense construct did not exhibit decreased syndecan-1 levels, indicating that loss of responsiveness to heparin-binding growth factors in these clones was not due to altered syndecan-1 expression. Furthermore, 8 of 10 tumors with stage 2 or 3 disease exhibited high levels of **glypican-1** by Northern blot anal. In contrast, low levels of **glypican-1** mRNA were evident in 1 of 10 tumors with stage 2 or 3 disease and in 9 of 10 tumors with stage 1 disease. Taken together, these data suggest that **glypican-1** may play a pivotal role in the ability of **breast cancer** cells to exhibit a mitogenic response to multiple heparin-binding growth factors and may contribute to disease progression in this malignancy.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2001:278289 CAPLUS
DOCUMENT NUMBER: 135:239988
TITLE: Enhanced glypican-3 expression differentiates the majority of hepatocellular carcinomas from benign hepatic disorders
AUTHOR(S): Zhu, Z-W.; Friess, H.; Wang, L.; Abou-Shady, M.; Zimmermann, A.; **Lander, A. D.**; **Korc, M.**; Kleeff, J.; Buchler, M. W.
CORPORATE SOURCE: Department of Visceral and Transplantation Surgery, University of Bern, Inselspital, Bern, Switz.
SOURCE: Gut (2001), 48(4), 558-564
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hepatocellular carcinoma (HCC) is a common malignant tumor worldwide, and its differential diagnosis from benign lesions of the liver is often difficult yet of great clin. importance. In the present study, we analyzed whether glypican-3 is useful in differentiating between benign and malignant liver diseases and whether it influences the growth behavior of HCC. Northern blot anal. indicated that expression of glypican-3 mRNA was either low or absent in normal liver, in focal nodular hyperplasia (FNH), and in liver cirrhosis. In contrast, expression of glypican-3 mRNA was markedly increased in 20 of 30 and moderately increased in five of 30 HCC samples. The average increase in glypican-3 mRNA expression in HCC was significant compared with expression in normal liver (21.7-fold increase, $p<0.01$). In comparison with FNH or liver cirrhosis, glypican-3 mRNA expression in HCC was increased 7.2-($p<0.05$) and 10.8-fold ($p<0.01$), resp. In addition, pushing HCCs exhibited significantly higher glypican-3 mRNA expression than invading tumors ($p<0.05$). In situ hybridization anal. demonstrated weak expression of glypican-3 mRNA in normal hepatocytes and bile ductular cells, and weak to occasionally moderate signals in hepatocytes forming nodules of liver cirrhosis and in regenerated hepatic nodules of FNH. In contrast, glypican-3 in situ hybridization signals were intense in hepatic cancer cells with even higher levels in pushing HCCs than in invading HCCs. These findings suggest that glypican-3, in many cases, has the potential to differentiate between benign and malignant liver diseases.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2000:277880 CAPLUS
DOCUMENT NUMBER: 132:305482
TITLE: Glypicans for the detection and treatment of human carcinoma
INVENTOR(S): **Lander, Arthur; Korc, Murray**
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023109	A1	20000427	WO 1999-US24176	19991015
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346264	AA	20000427	CA 1999-2346264	19991015
EP 1146903	A1	20011024	EP 1999-954963	19991015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

AU 769125	B2	20040115	AU 2000-11181		19991015
US 2003103980	A1	20030605	US 2002-210327		20020731
PRIORITY APPLN. INFO.:			US 1998-104510P	P	19981016
			US 1999-121624P	P	19990225
			WO 1999-US24176	W	19991015
			US 2001-807575	A2	20010712
			US 2001-309722P	P	20010731

AB Glycosylphosphatidylinositol- (GPI-) anchored **HSPG** **glypican-1** is strongly expressed in human **breast** and **pancreatic cancer** - both by the **cancer** cells and in the case of **pancreatic cancer** the adjacent fibroblasts - whereas expression of **glypican-1** is low in the normal **pancreas** and in chronic **pancreatitis**. Treatment of two **pancreatic cancer** cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 **breast cancer** cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in **breast cancer** tissues as well as **breast cancer** cells by comparison with **breast** normal tissues. Temporary or permanent transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein levels and the mitogenic response to FGF2 and HB-EFG. Glypican can be used to detect the carcinoma in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense constructs) of surface of the extracellular domain of **glypican-1** are effective in retarding the growth of glypican-responsive carcinomas.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

ACCESSION NUMBER:	2000:670459 CAPLUS
DOCUMENT NUMBER:	134:145417
TITLE:	Syndecan-1 expression is up-regulated in **pancreatic** but not in other gastrointestinal **cancers**
AUTHOR(S):	Conejo, J. R.; Kleeff, J.; Koliopanos, A.; Matsuda, K.; Zhu, Z. W.; Goecke, H.; Bicheng, N.; Zimmermann, A.; **Korc, M.**; Friess, H.; Buchler, M. W.
CORPORATE SOURCE:	Department of Visceral and Transplantation Surgery, University of Bern, Bern, CH-3010, Switz.
SOURCE:	International Journal of Cancer (2000), 88(1), 12-20 CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER:	Wiley-Liss, Inc.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Syndecan-1 belongs to the syndecan family of cell surface transmembrane **heparan-sulfate proteoglycans**, which participate in cell proliferation, cell migration, and cell-matrix interactions. Decreased expression of syndecan-1 has been observed in some gastrointestinal malignancies, and it is thought that high levels of syndecan-1 correlate with the maintenance of epithelial morphol. and inhibition of invasiveness. Here, the expression of syndecan-1 was characterized in normal, chronic **pancreatitis**, and primary and metastatic human **pancreatic cancer** tissues; in cultured **pancreatic cancer** cell lines; and in esophageal, gastric, colon, and liver **cancers**. **Pancreatic cancer** cell lines expressed syndecan-1 mRNA and protein at variable levels. In addition, these cells also released syndecan-1 into the culture medium. **Pancreatic cancer** tissues markedly over-expressed syndecan-1 mRNA in comparison with both chronic **pancreatitis** (2.4-fold increase) and normal **pancreatic** samples (10.6-fold increase). There was no difference in syndecan-1 mRNA expression between early and advanced tumors. By in situ hybridization and immunohistochem., syndecan-1 expression was evident at relatively low levels in the ductal cells and less frequently in acinar cells of the normal pancreas. In chronic pancreatitis, syndecan-1 was present at low to moderate levels in areas with atrophic acinar cells and ductular complexes. In contrast, in **pancreatic cancer** tissues, syndecan-1 was present at moderate to high levels in the majority of the **cancer** cells within the **tumor** mass and also in metastatic lesions of **pancreatic tumors**. Syndecan-1 mRNA levels in other gastrointestinal malignancies (esophageal, gastric, colon and liver cancers) were not different from the levels observed in the corresponding normal samples. Together, the findings suggest that syndecan-1 expression by **pancreatic cancer** cells may be of importance in the pathobiol. of this disorder and that its role in **pancreatic cancer** seems to be different from that in other gastrointestinal malignancies.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1999:735682 CAPLUS
DOCUMENT NUMBER: 133:15482
TITLE: Characterization of cytokeratin 20 expression in pancreatic and colorectal cancer
AUTHOR(S): Wildi, Stefan; Kleeff, Jorg; Maruyama, Haruhisa; Maurer, Christoph A.; Friess, Helmut; Buchler, Markus W.; **Lander, Arthur D.**; **Korc, Murray**
CORPORATE SOURCE: Departments of Medicine, Biological Chemistry, and Pharmacology, University of California, Irvine, CA, 92697, USA
SOURCE: Clinical Cancer Research (1999), 5(10), 2840-2847
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytokeratin 20 belongs to the epithelial subgroup of the intermediate filament family. Because of its restricted range of expression in humans, it has become an important tool for detecting and identifying metastatic cancer cells by immunohistochem. and by PCR anal. Despite its widespread diagnostic use in colorectal cancer and occasional use in pancreatic cancer, little is known about the expression of CK 20 in these tumors in vivo. Therefore, in the present study we characterized CK 20 expression in pancreatic and colorectal cancer by comparison with its expression in the normal pancreas and colon. Tissue samples from 24 patients with pancreatic cancer and from 41 patients with colorectal cancer were examined for CK 20 expression by Northern blot anal., immunohistochem., and in situ hybridization. CK 20 expression was observed in the cancer cells of both cancer types. A subgroup of the pancreatic cancers exhibited a 3.2-fold increase in CK 20 mRNA by comparison with resp. normal controls. In contrast, colon cancers underexpressed CK 20 mRNA by comparison with the resp. controls. In the normal tissues, CK 20 immunoreactivity was relatively faint and sparse in the pancreatic ductal cells but intense and abundant in the apical portions of the colonic mucosa. CK 20 immunoreactivity was also evident in the ductal cells from the chronic pancreatitis-like lesions adjacent to the cancer cells. Furthermore, distant metastases from pancreas carcinomas exhibited strong CK 20 immunoreactivity. It is concluded that CK 20 is overexpressed in pancreatic cancer and that it can serve as an excellent marker for metastatic pancreatic cancer.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 13 OF 15 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 1999433578 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10505759
TITLE: Stable transfection of a **glypican-1** antisense construct decreases tumorigenicity in PANC-1 **pancreatic carcinoma** cells.
AUTHOR: Kleeff J; Wildi S; Kumbasar A; Friess H; **Lander A D; Korc M**
CORPORATE SOURCE: Department of Medicine, University of California, Irvine 92697, USA.
CONTRACT NUMBER: CA-40162 (NCI)
SOURCE: Pancreas, (1999 Oct) Vol. 19, No. 3, pp. 281-8. Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991123

AB **Glypican-1** belongs to a family of glycosylphosphatidylinositol (GPI)-anchored **heparan sulfate proteoglycans** (**HSPGs**) that affect cell growth, invasion, and adhesion. Cell-surface **HSPGs** are believed to act as co-receptors for heparin-binding mitogenic growth factors. It was reported that **glypican-1** is strongly expressed in human **pancreatic cancer**, and that it may play an essential role in regulating growth-factor responsiveness in **pancreatic carcinoma** cells. In

this study we investigated the effects of decreased **glypican -1** expression in PANC-1 **pancreatic cancer** cells. To this end, PANC-1 cells were stable transfected with a full-length **glypican-1** antisense construct. The glypican- antisense transfected clones displayed markedly reduced glypican- protein levels and a marked attenuation of the mitogenic responses to heparin-binding growth factors that are commonly overexpressed in **pancreatic cancer**: fibroblast growth factor-2 (FGF2), heparin-binding epidermal growth factor (EGF)-like growth factor (HB-EGF), and hepatocyte growth factor (HGF). In addition, **glypican-1** antisense-expressing PANC-1 cells exhibited a significantly reduced ability to form tumors in nude mice in comparison with parental and sham-transfected PANC-1 cells. These data suggest that **glypican-1** plays an important role in the responses of **pancreatic cancer** cells to heparin-binding growth factors, and documents for the first time that its expression may enhance tumorigenic potential in vivo.

L32 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 1998:727948 CAPLUS
DOCUMENT NUMBER: 130:93698
TITLE: The cell-surface **heparan sulfate proteoglycan glypican-1** regulates growth factor action in **pancreatic carcinoma** cells and is overexpressed in human **pancreatic cancer**
AUTHOR(S): Kleeff, Jorg; Ishiwata, Toshiyuki; Kumbasar, Asli; Friess, Helmut; Buchler, Markus W.; **Lander, Arthur D.; Korc, Murray**
CORPORATE SOURCE: Departments of Medicine, Biological Chemistry, and Pharmacology, University of California, Irvine, CA, 92697, USA
SOURCE: Journal of Clinical Investigation (1998), 102(9), 1662-1673
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Heparan sulfate proteoglycans** (**HSPGs**) play diverse roles in cell recognition, growth, and adhesion. In vitro studies suggest that cell-surface **HSPGs** act as coreceptors for heparin-binding mitogenic growth factors. Here the authors show that the glycosylphosphatidylinositol- (GPI-) anchored **HSPG glypican-1** is strongly expressed in human **pancreatic cancer**, both by the **cancer** cells and the adjacent fibroblasts, whereas expression of **glypican-1** is low in the normal **pancreas** and in chronic **pancreatitis**. Treatment of two **pancreatic cancer** cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors that are commonly overexpressed in **pancreatic cancer**: fibroblast growth factor 2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). PI-PLC did not alter the response to the non-heparin-binding growth factors EGF and IGF-1. Stable expression of a form of **glypican-1** engineered to possess a transmembrane domain instead of a

GPI anchor conferred resistance to the inhibitory effects of PI-PLC on growth factor responsiveness. Furthermore, transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein levels and the mitogenic response to FGF2 and HB-EGF. The authors propose that **glypican-1** plays an essential role in the responses of **pancreatic cancer** cells to certain mitogenic stimuli, that it is relatively unique in relation to other **HSPGs**, and that its expression by **pancreatic cancer** cells may be of importance in the pathobiol. of this disorder.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 15 OF 15 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 1998364663 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9700949
TITLE: Role of fibroblast growth factors and their receptors in **pancreatic cancer** and chronic **pancreatitis**.
AUTHOR: Kornmann M; Beger H G; **Korc M**
CORPORATE SOURCE: Department of Medicine, Biological Chemistry and Pharmacology, University of California, Irvine, USA.
SOURCE: Pancreas, (1998 Aug) Vol. 17, No. 2, pp. 169-75. Ref: 71
Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981020

AB The fibroblast growth factor (FGF) family is a group of homologous heparin-binding polypeptides that has been implicated in a variety of human neoplasms and presently includes 14 members. FGF signaling is mediated by a dual-receptor system, consisting of four high-affinity tyrosine kinase receptors, termed fibroblast growth factor receptors (FGFRs), and of low-affinity **heparan sulfate proteoglycan** receptors that enhance ligand presentation to the FGFRs. Several FGFs, including FGF-1, -2, -3, -4, -5, -6, and -7, and several FGFR variants, among them the 2 immunoglobulin-like form and the IIIc splice variant of FGFR-1 and the keratinocyte growth factor receptor, a splice variant of FGFR-2, are expressed in human **pancreatic cancer** cell lines and are overexpressed in human **pancreatic cancers** or in the **pancreas** of chronic **pancreatitis** and, therefore, may play important roles in the pathobiology of these **pancreatic** diseases. This review summarizes the current information on the involvement of the FGF family and their receptors in human **pancreatic cancer** and chronic **pancreatitis**

=> fil hom
FILE 'HOME' ENTERED AT 17:51:55 ON 16 MAR 2006

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=> d his ful

     (FILE 'REGISTRY' ENTERED AT 17:22:23 ON 16 MAR 2006)
                DEL HIS Y
                E "GLYPICAN-1"/CN
                E GLYPICAN 1/CN
L1            2 SEA ABB=ON  PLU=ON  ("GLYPICAN 1 (HUMAN)"/CN OR "GLYPICAN
                1 (MOUSE STRAIN C57BL/6 CLONE MGC:86094 IMAGE:6810413)"/CN)

                E "GLYPICAN-I"/CN
                E GLYPICAN I/CN

     FILE 'CAPLUS' ENTERED AT 17:23:42 ON 16 MAR 2006
L*** DEL      7 S (KORC M? AND LANDER A?)/AU
L*** DEL      6 S L2 AND GLYPICAN
L*** DEL      6 S L3 AND ?CANCER?
                D TI AU 1-6
                D .BEVSTR1 2
L2         3313 SEA ABB=ON  PLU=ON  L1 OR GLYPICAN(1W)(1 OR I) OR HSPG OR
                HEPARAN(W)(SULFATE OR SULPHATE)(W)(PROTEOGLYCAN OR PROTEO
                GLYCAN) OR (PROTEOHEPARAN OR PROTEO HEPARAN)(W)(SULFATE OR
                SULPHATE)
L3           85 SEA ABB=ON  PLU=ON  L2 AND (CANCER? OR CARCIN? OR TUMOUR
                OR TUMOR OR NEOPLAS?)(S)(PANCREAS OR PANCREAT? OR BREAST
                OR MAMMAR?)
L4           33 SEA ABB=ON  PLU=ON  L3 AND (DIAGNOS? OR DETECT? OR DET##
                OR DETERM? OR SCREEN?)
                D KWIC
L5           14 SEA ABB=ON  PLU=ON  L2 AND (DIAGNOS? OR DETECT? OR DET##
                OR DETERM? OR SCREEN?)(S)((CANCER? OR CARCIN? OR TUMOUR OR
                TUMOR OR NEOPLAS?)(10A)(BREAST OR MAMMAR? OR PANCREAT? OR
                PANCREAS))

     FILE 'REGISTRY' ENTERED AT 17:31:38 ON 16 MAR 2006

     FILE 'CAPLUS' ENTERED AT 17:31:38 ON 16 MAR 2006
                D QUE L5
                D L5 1-14 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 17:31:41 ON 16 MAR 2006
L6           37 SEA ABB=ON  PLU=ON  L5
L7           17 DUP REM L6 (20 DUPLICATES REMOVED)
                D 1-17 IBIB ABS

     FILE 'CAPLUS' ENTERED AT 17:34:10 ON 16 MAR 2006
L8          131 SEA ABB=ON  PLU=ON  HS(W)(PROTEOGLYCAN OR PROTEO GLYCAN)
L9            1 SEA ABB=ON  PLU=ON  L8 AND (DIAGNOS? OR DETECT? OR DET##
                OR DETERM? OR SCREEN?)(S)((CANCER? OR CARCIN? OR TUMOUR OR
                TUMOR OR NEOPLAS?)(10A)(BREAST OR MAMMAR? OR PANCREAT? OR
                PANCREAS))
L10           0 SEA ABB=ON  PLU=ON  L9 NOT L5

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 17:36:07 ON 16 MAR 2006
L11           4 SEA ABB=ON  PLU=ON  L9
L12           0 SEA ABB=ON  PLU=ON  L11 NOT L6

     FILE 'CAPLUS' ENTERED AT 17:38:21 ON 16 MAR 2006
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L13          249 SEA ABB=ON  PLU=ON  (L2 OR L8)(S)ANTIBOD?
L14            3 SEA ABB=ON  PLU=ON  L13 AND (CANCER? OR CARCIN? OR TUMOUR
                 OR TUMOR OR NEOPLAS?)(S)(PANCREAS OR PANCREAT? OR BREAST
                 OR MAMMAR?)
L15            0 SEA ABB=ON  PLU=ON  L14 NOT L5

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 17:40:24 ON 16 MAR 2006
L16           27 SEA ABB=ON  PLU=ON  L14
L17           21 SEA ABB=ON  PLU=ON  L16 AND (DIAGNOS? OR DETECT? OR DET##
                 OR DETERM? OR SCREEN?)
L18           11 SEA ABB=ON  PLU=ON  L17 NOT L6
L19            8 DUP REM L18 (3 DUPLICATES REMOVED)
                 D L19 1-8 IBIB ABS

     FILE 'MEDLINE' ENTERED AT 17:43:30 ON 16 MAR 2006
                 E HEPARAN SULFATE PROTEOGLYCAN/CT
L20         1871 SEA ABB=ON  PLU=ON  "HEPARAN SULFATE PROTEOGLYCAN"/CT
                 E PANCREATIC NEOPLASMS/CT 5
L21        32072 SEA ABB=ON  PLU=ON  "PANCREATIC NEOPLASMS"/CT
                 E BREAST NEOPLASMS/CT 5
L22       131008 SEA ABB=ON  PLU=ON  "BREAST NEOPLASMS"/CT
L23           22 SEA ABB=ON  PLU=ON  L20 AND (L21 OR L22)
L24            0 SEA ABB=ON  PLU=ON  L23 AND (DIAGNOSIS OR DIAGNOSTIC
                 USE)/CT
                 D QUE L24
                 D L23 1-22 .BEVERLYMED

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 17:45:46 ON 16 MAR 2006
L25         1453 SEA ABB=ON  PLU=ON  "KORC M"?/AU
L26          540 SEA ABB=ON  PLU=ON  "LANDER A"?/AU
L27           34 SEA ABB=ON  PLU=ON  L25 AND L26
L28         1959 SEA ABB=ON  PLU=ON  L25 OR L26
L29          167 SEA ABB=ON  PLU=ON  L28 AND (L2 OR L8)
L30           43 SEA ABB=ON  PLU=ON  L29 AND (CANCER? OR CARCIN? OR TUMOUR
                 OR TUMOR OR NEOPLAS?)(S)(PANCREAS OR PANCREAT? OR BREAST
                 OR MAMMAR?)
L31           54 SEA ABB=ON  PLU=ON  L27 OR L30
L32           15 DUP REM L31 (39 DUPLICATES REMOVED)
                 D 1-15 IBIB ABS

     FILE 'HOME' ENTERED AT 17:51:55 ON 16 MAR 2006


     FILE CAPLUS

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     FILE COVERS 1907 - 16 Mar 2006  VOL 144 ISS 12
     FILE LAST UPDATED: 15 Mar 2006  (20060315/ED)

                    Searcher    :     Shears     571-272-2528
```

Effective October 17, 2005, revised CAS Information Use Policies apply
They are available for your review at:

http://www.cas.org/infopolicy.html

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 15 MAR 2006 HIGHEST RN 877033-93-7
DICTIONARY FILE UPDATES: 15 MAR 2006 HIGHEST RN 877033-93-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMI
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE MEDLINE
FILE LAST UPDATED: 16 MAR 2006 (20060316/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details
on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 15 March 2006 (20060315/ED)

FILE EMBASE
FILE COVERS 1974 TO 10 Mar 2006 (20060310/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

The updates on February 20 and 24, 2006, were incomplete due to a technical problem. The problem has been corrected, and the missing records were included in the update on March 3, 2006. If you received SDI results from the original updates on February 20 and 24, you will automatically be credited for the update that was rerun on March 3.

If you have any questions, please contact your STN Service Center.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 15 MAR 2006 <20060315/UP>
MOST RECENT DERWENT UPDATE: 200618 <200618/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://scientific.thomson.com/support/products/dwpi/

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS:
http://scientific.thomson.com/support/products/dwpifv/

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
PLEASE CHECK:
http://scientific.thomson.com/support/patents/dwpiref/reftools/classif

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

FILE CONFSCI

FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

CSA has suspended updates until further notice.

FILE SCISEARCH

FILE COVERS 1974 TO 9 Mar 2006 (20060309/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 13 MAR 2006 (20060313/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE COVERS APR 1973 TO OCTOBER 27, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE.
USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHE
DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION
ABOUT THE IPC REFORM <<<

FILE HOME